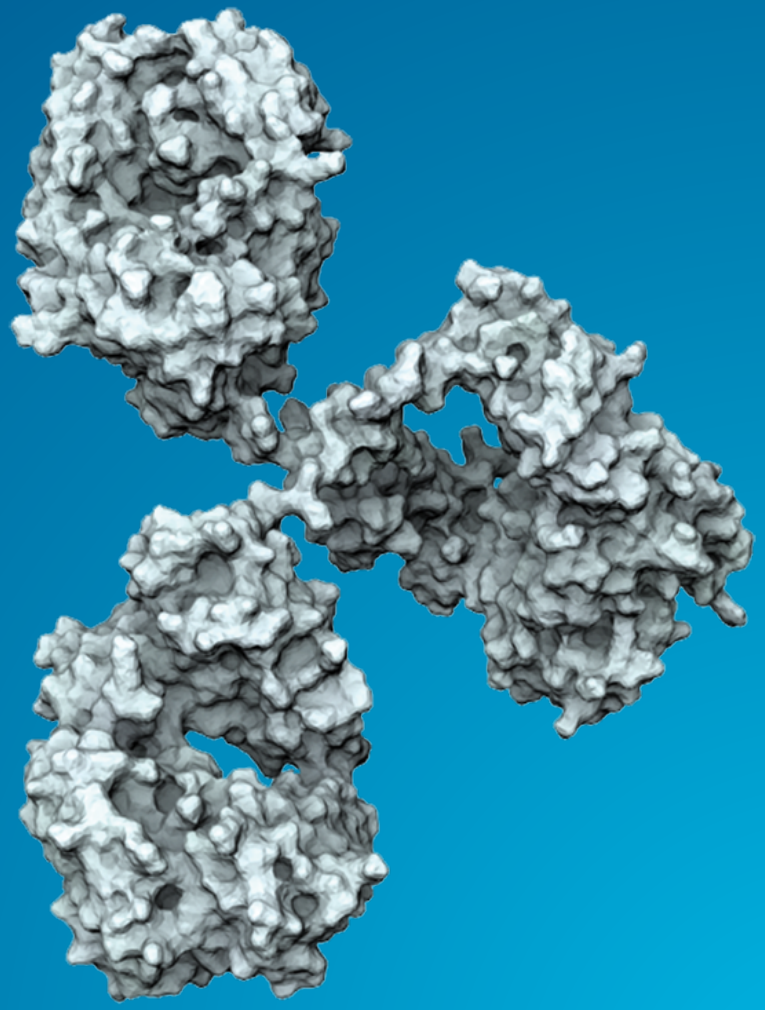
Translating **science** into **global** health impact

IAVI-Wellcome Global Call to Action: Expanding Access to Monoclonal Antibody-based Products



Ayesha Sitlani, Ph.D

IAVI, Associate Vice President - Antibody Strategy

Global Health Centre, Graduate Institute of Geneva,
November 25, 2020

IAVI gratefully acknowledges the generous support provided by the following major donors

PEPFAR U.S. President's Emergency Plan for AIDS Relief

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Ministry of Science & Technology
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CEPI | New vaccines for a safer world

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wellcome

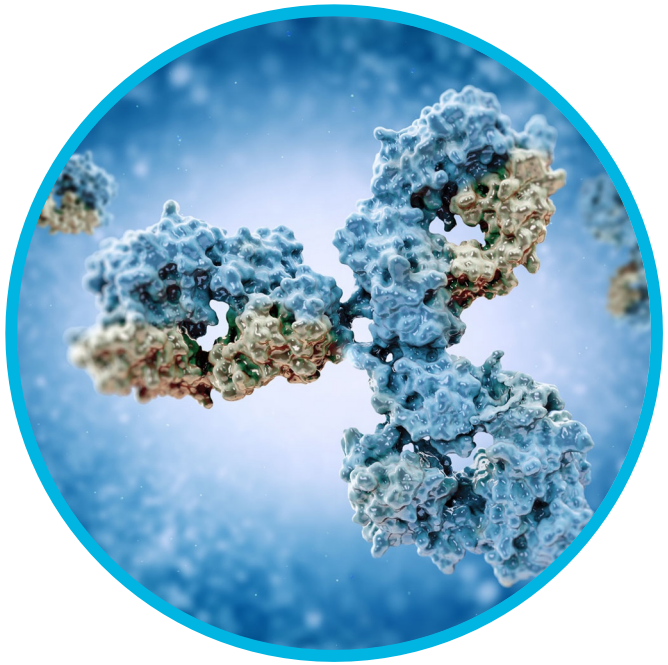
The Research Council of Norway

Foundation for the National Institutes of Health | National Institute of Allergy and Infectious Diseases | amfAR, The Foundation for AIDS Research | The Buimerc Group | Broadway Cares/Equity Fights AIDS | Cancer Research UK | The City of New York, Economic Development Corporation | Congressionally Directed Medical Research Program (DoD) | GSK | The Hearst Foundations | Keith Haring Foundation | Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the USA and Canada)

And many other generous individuals and partners around the world

As of September 2020

IAVI: Where discovery, scientific partnerships, and global access meet



IAVI brings together in-house researchers on infectious and neglected diseases, public and private partners, and local communities to develop and deliver vaccines and antibodies that are affordable and globally accessible

Expanding Access to Monoclonal Antibody-based Products: A Global Call to Action

IAVI-authored, Wellcome-commissioned call to action - published 10 August 2020

- Analyses of the **gaps and opportunities** for global access to antibodies for all diseases, with a focus on LMICs
- Formulate a **series of recommended actions** to expand global access to antibodies
- **Comes at a critical time**: the pandemic has triggered unprecedented collaboration on mAbs to prevent and treat COVID-19

Available at iavi.org and wellcome.org/reports/expanding-access-monoclonal-antibodies

Expanding Access to Monoclonal Antibody-based Products: A Global Call to Action

Main Report (plus 5 supplements) - A Global Call to Action – series of recommendations to expand access to mAbs

Method:

- **Peer-reviewed biomedical literature**, news sources, recognized global and national datasets/registries/reports
- **Case studies** of marketed antibodies for non-communicable diseases, infectious and neglected diseases
- Series of more than **>100 stakeholder interviews across > 15 countries** with global-health organizations, government agencies/ funders, academic institutions, regulatory authorities, product developers, bio-pharmaceutical companies, philanthropic organizations, NGO/ civil societies
- **Group stakeholder meetings** were convened in India, sub-Saharan Africa (SSA) and in several high-income countries

Global Stakeholders - Interviews

Academic and Public Research Institutions

Indian Institute of Technology (IIT), India
Translational Health Science and Technology Institute (THSTI), India
Institute of Chemical Technology (ICT), India
Indian Institute of Technology, India
National Institute of Immunology (NII), India
University of Delhi, India
Indian Institute of Science (IISc), Bangalore, India
Jawaharlal Nehru Centre for Advanced Scientific Research(JNCASR), India
Council of Scientific & Industrial Research—Central Drug ResearchInstitute (CSIR-CDRI), India
Regional Centre for Biotechnology, India
Institute of Microbial Technology (IMTECH), Chandigarh, India
Centre for Cellular and Molecular Platforms (C-CAMP), India

Centre for the AIDS Programme of Research in South Africa (CAPRISA), South Africa
KEMRI – Wellcome Trust, Initiative to Develop African Research Leaders (IDeAL), Kenya
University of Zambia School of Medicine, Zambia

Massachusetts Institute of Technology (MIT), MA(BioAccess Global Health Initiative), US
ICAP at Columbia University, US
St. George's, University of London, UK

Biopharmaceutical

Adimab, US
Kymab, UK
Mapp Biopharmaceutical, US
Johnson & Johnson, US
GSK, UK
Merck, US
Novartis, Switzerland
Pfizer, US
Regeneron, US
Roche, Switzerland
Sanofi, France
Takeda, Japan

Gennova Biopharmaceuticals, India
Anthem Biosciences, India
Syngene International, India
Serum Institute of India, Pvt. Ltd (SIIPL), India
Cipla, India
Lupin, India
Cadila Pharmaceuticals, India
Biocon, India
Clonz Biotech, India
International Health Management Associates, India

Global Stakeholders - Interviews

Government Agency/Funder

Biotechnology Industry Research Assistance Council (BIRAC), India
Department of Biotechnology, Government of India, India

National AIDS & STI Control Programme (NASCOP), Kenya
Kenya Ministry of Health Pharmacy and Poisons Board, Kenya
National Hospital Insurance Fund (NHIF), Kenya

U.S. President's Emergency Plan for AIDS Relief (PEPFAR), US
Defense Advanced Research Projects Agency (DARPA), US
United States Agency for International Development (USAID), US

Non-governmental organizations/ Civil society

Campaigning for Cancer, South Africa
Southern African Generic Medicines Association (SAGMA),South Africa
Treatment Action Group (TAG), US
Southern African Programme on Access to Medicines (SAPAM),South Africa
Southern African Development Community (SADC), Botswana

Regulatory agency/ institution

African Vaccine Manufacturing Initiative (AVMI), South Africa
European Medicines Agency (EMA), EU
U.S. Food and Drug Administration (USFDA), US

Multilateral/ United Nations/ Global health organizations

Gavi, The Vaccine Alliance, Switzerland
Medicines for Malaria Venture (MMV), Switzerland
Unitaid, Switzerland
The Global Fund to Fight AIDS, Tuberculosis and Malaria, Switzerland
Access to Medicines Foundation (AMF), Netherlands
Joint United Nations Programme on HIV/AIDS (UNAIDS), Switzerland
Medicines Patent Pool (MPP), Switzerland
United Nations International Children's Fund (UNICEF), US
World Health Organization (WHO), Switzerland

Non-profit product developers/ PDPs

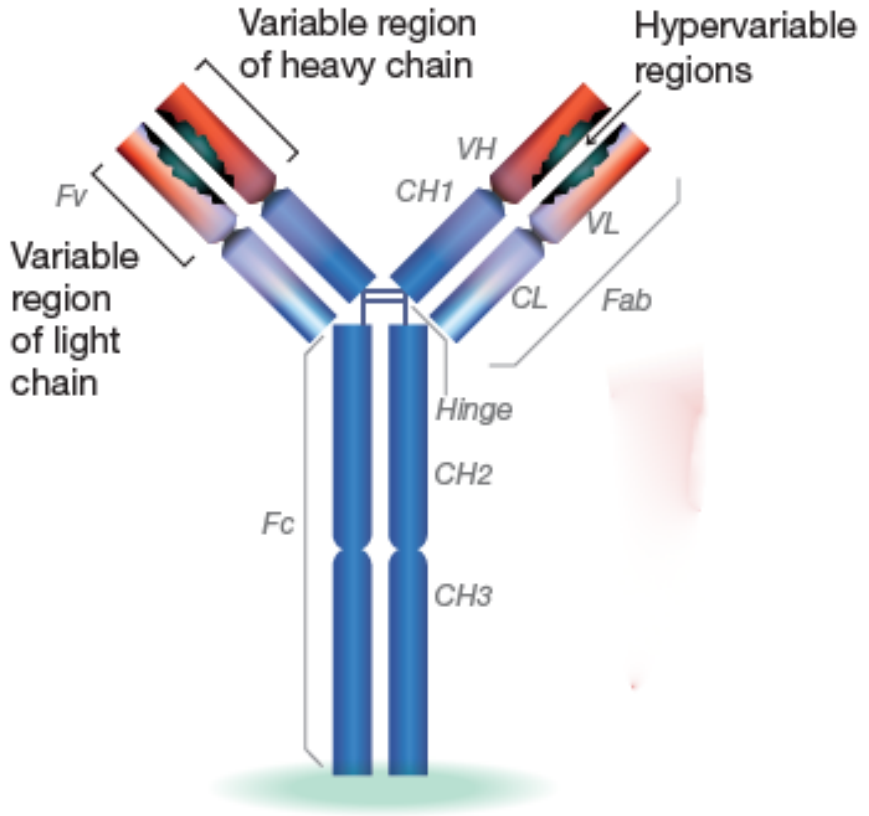
Butantan Institute & Foundation, Brazil
Utrecht Centre for Affordable Biologics (UCAB), Netherlands
PATH, US
IAVI, US

Philanthropic organizations

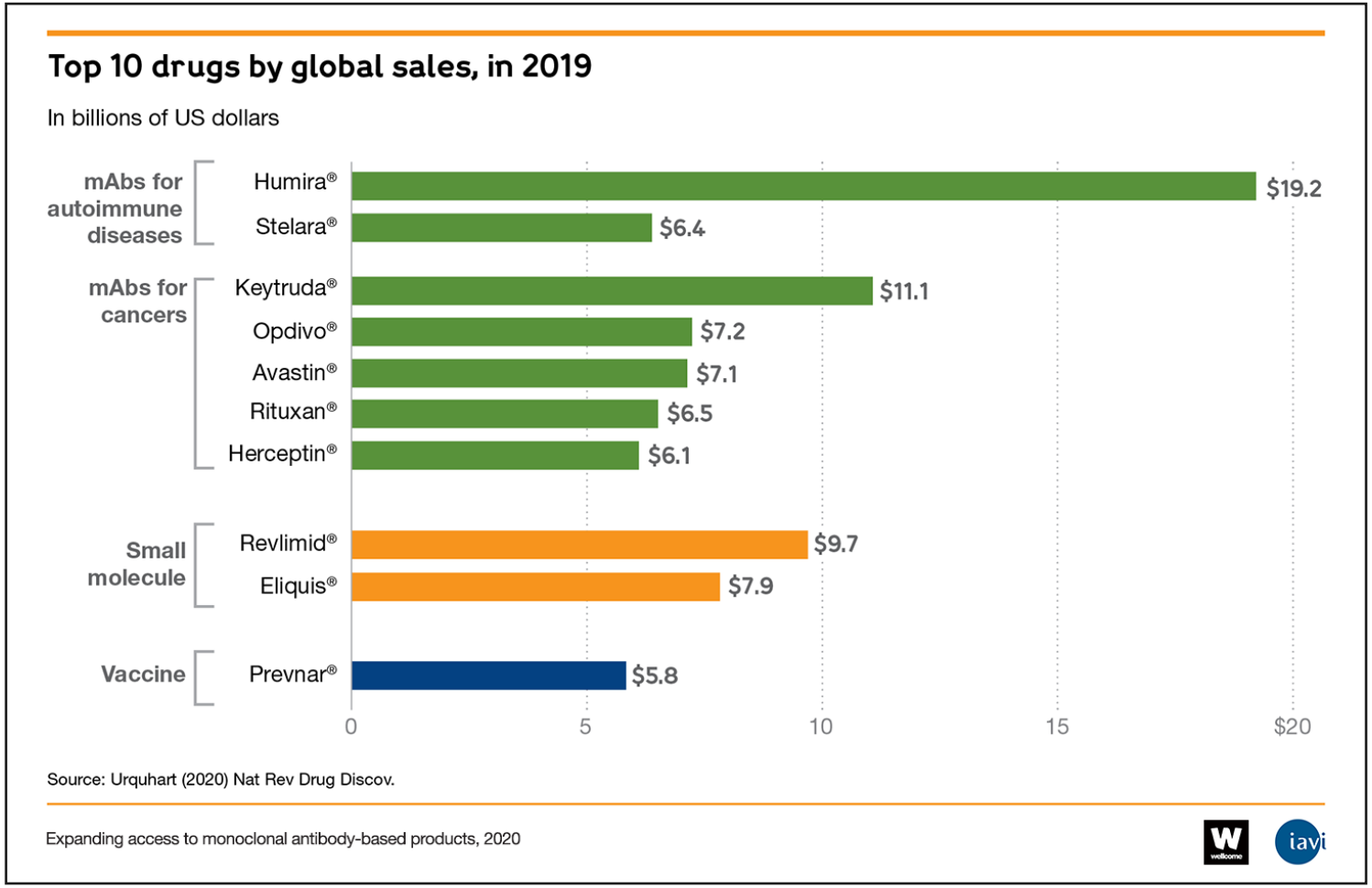
Bill & Melinda Gates Foundation (BMGF), US
Clinton Health Access Initiative (CHAI), US
Wellcome (UK)

What are Monoclonal Antibodies?

- Antibodies are proteins generated by the immune system
- They are one of the primary ways the body defends itself against disease
- They bind specifically to their targets (viruses, bacteria, cancer cells, etc.) and interfere with their pathogenic effects or flag them for destruction
- Most licensed vaccines induce antibodies against specific pathogens
- ***Monoclonal antibodies (mAbs) are single antibodies expressed from identical immune cells that can be manufactured at commercial scale using cell systems***
- **Mabs are a powerful tool in treating and preventing disease and are generally safer than small molecule drugs**



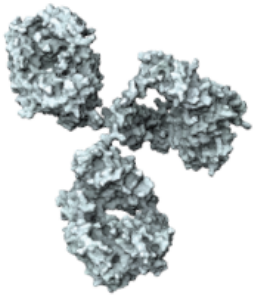
Monoclonal Antibodies (mAbs) for Non-Communicable Diseases (NCDs): 7 of the top 10 drugs by global sales

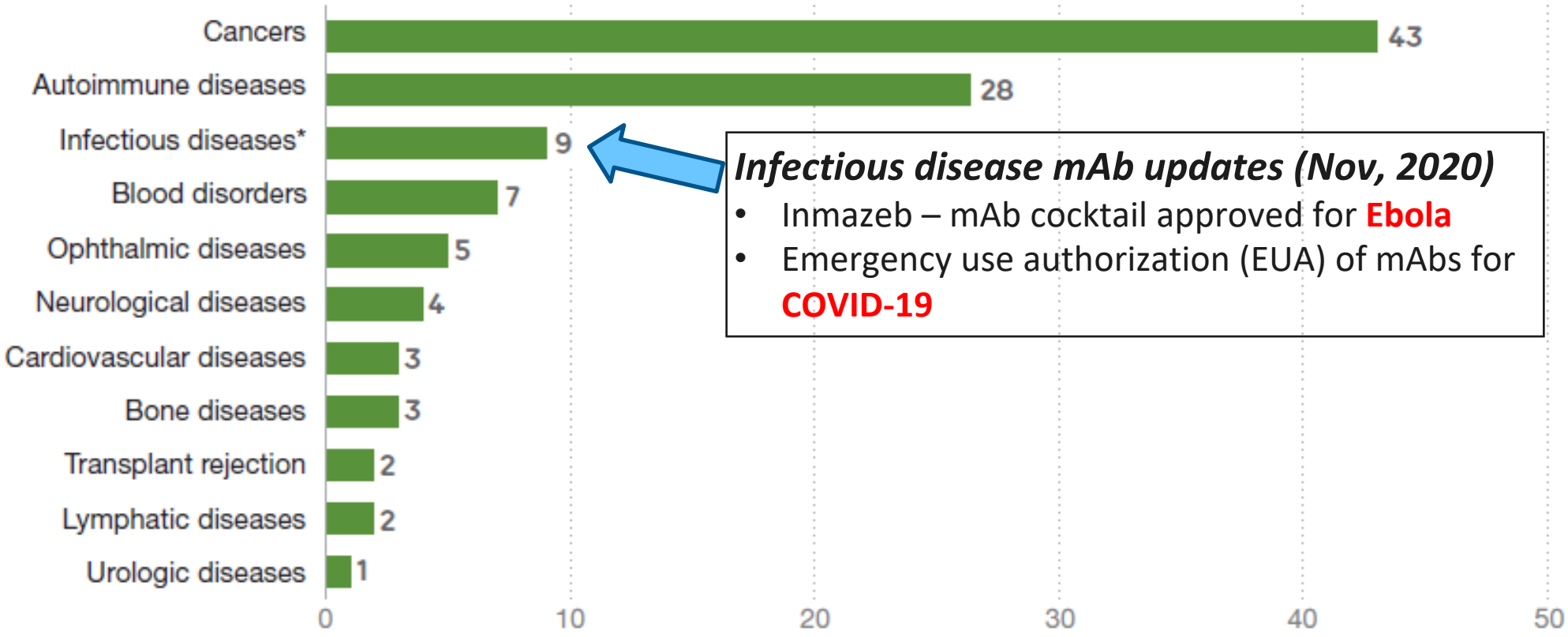


Limited access to mAbs for NCDs in low- and middle-income countries

- Majority of deaths from NCDs occur in LMICs, with a rapid rate of increase
- Cancer services and access to diagnostic medical equipment are limited in LMICs
- Unclear assessment of disease burden and market size in LMICs

Monoclonal Antibodies for the treatment and prevention of diseases – approved or under review in the US and EU





Infectious disease mAb updates (Nov, 2020)

- Inmazeb – mAb cocktail approved for **Ebola**
- Emergency use authorization (EUA) of mAbs for **COVID-19**

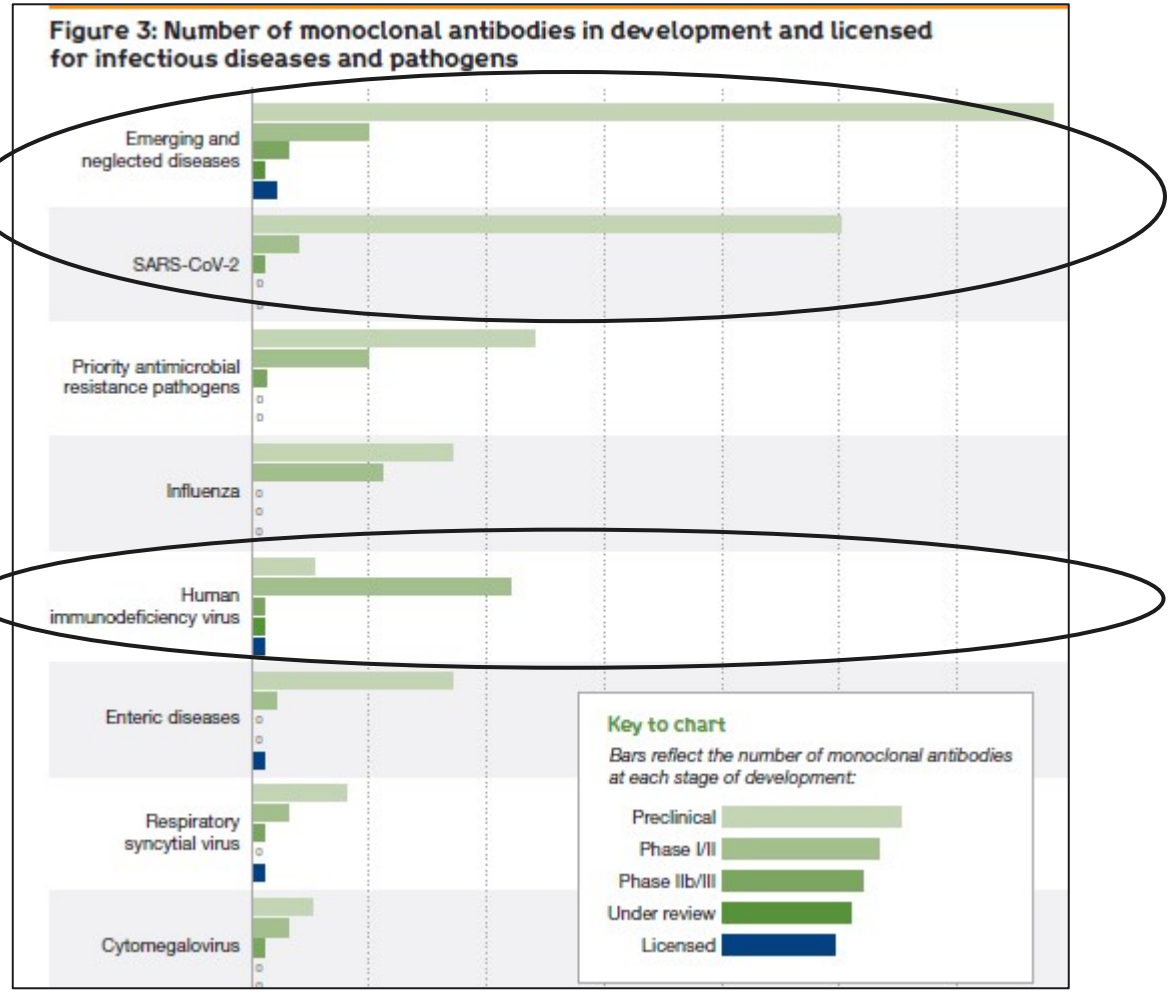
*Infectious diseases mAbs include five licensed in US/EU, two licensed in India, and two novel mAbs under review.

Source: Reichert (2020), The Antibody Society (www.antibodysociety.org)

Percentage of antibodies in R&D pipeline doubled in the past 20 years – currently at 40%

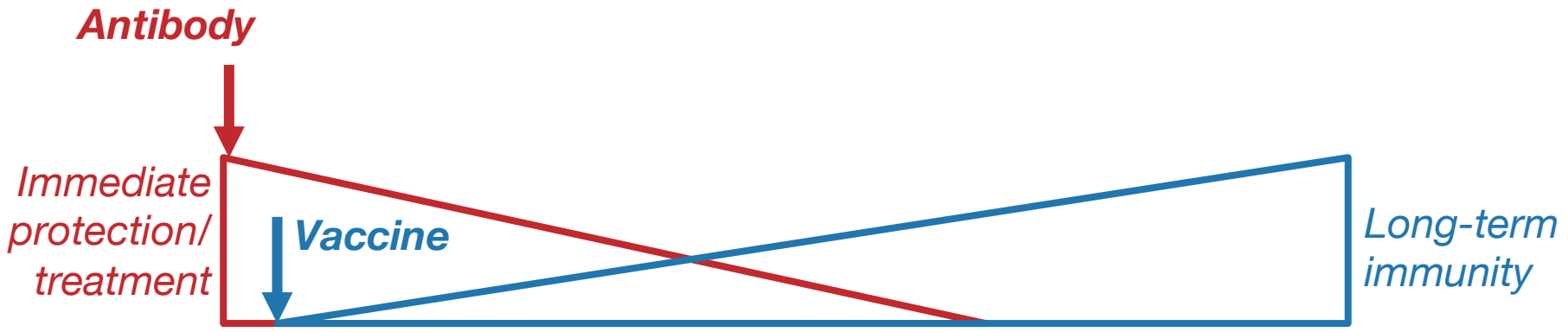
Several promising antibodies in clinical development for Infectious and Neglected Diseases, including COVID-19, making global access a priority

- More than **350** mAbs in the pipeline for infectious and neglected diseases
  - preclinical programs include *Ebola, Sudan, Marburg, Nipah, Hendra, MERS, Dengue, Zika, Chikungunya, Junin, Lassa, Rabies, Snakebite*
  - ***More than 100 SARS-CoV-2 mAb programs in development***
  - ***18 SARS-CoV-2 mAb programs in the clinic, with 5 programs in Ph III***
  - ***Several HIV bnAb programs in development***



Antibodies are complementary interventions to Vaccines for Infectious Diseases

Immediate and long-term protection & treatment

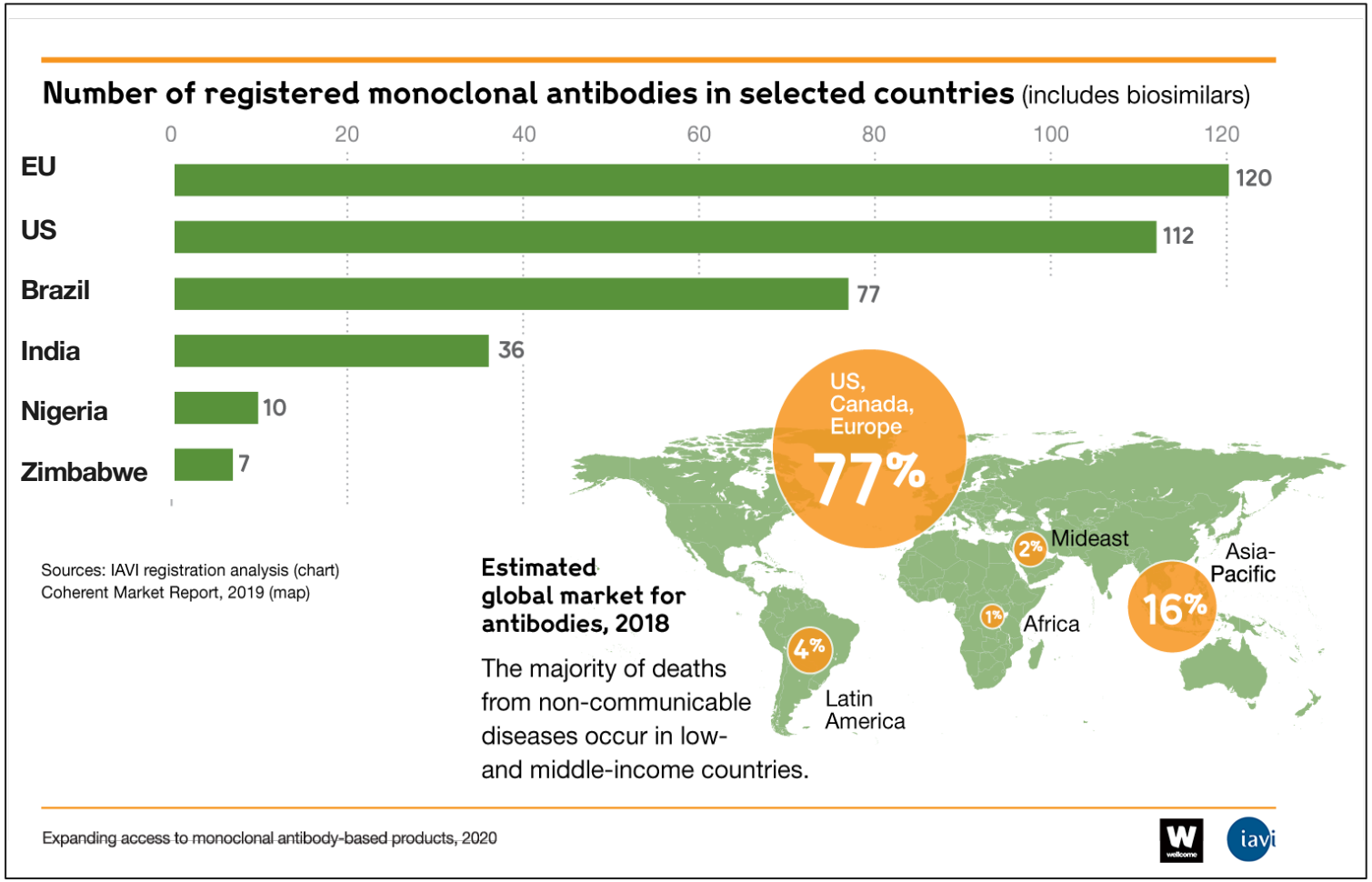


Populations protected/ treated

Monoclonal antibodies are more complex and expensive to develop and produce than small molecule generic drugs. And the business and partnership models that have vastly expanded global access to some HIV drugs are not necessarily applicable or sufficient. Ensuring monoclonal antibodies are available and affordable globally will require new ways of thinking, new types of collaboration and new ways of doing business.

IAVI-Wellcome, Expanding Access to Monoclonal Antibody-Based Products: A Global Call to Action, 2020

Monoclonal Antibodies (mAbs) have revolutionized treatment for many diseases, but global access is severely limited



Access to antibody-based products in LMICs, is severely limited and this ***access gap is expected to widen*** as the proportion of antibodies in product pipelines continues to increase

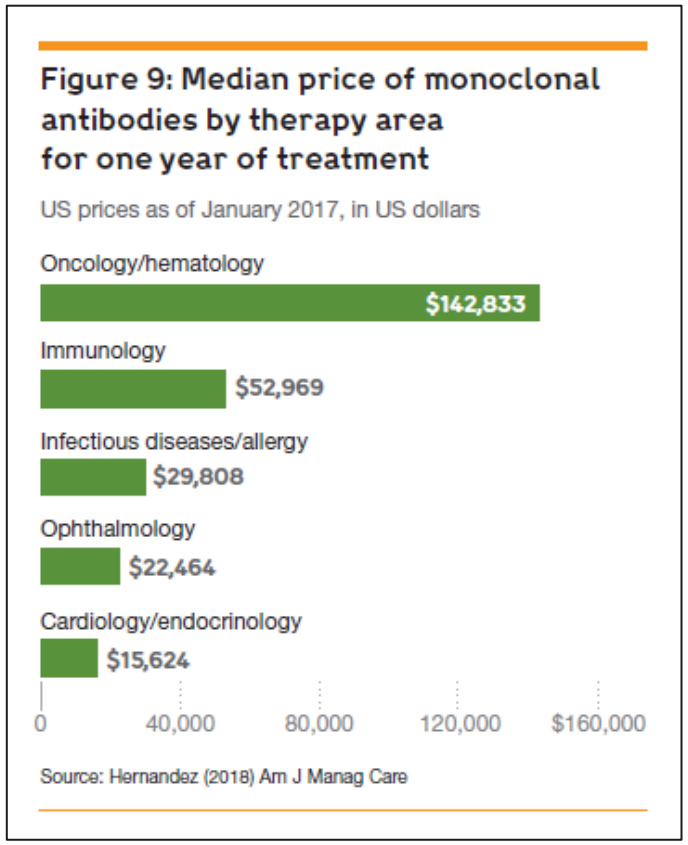
Lack of **availability** and **affordability**

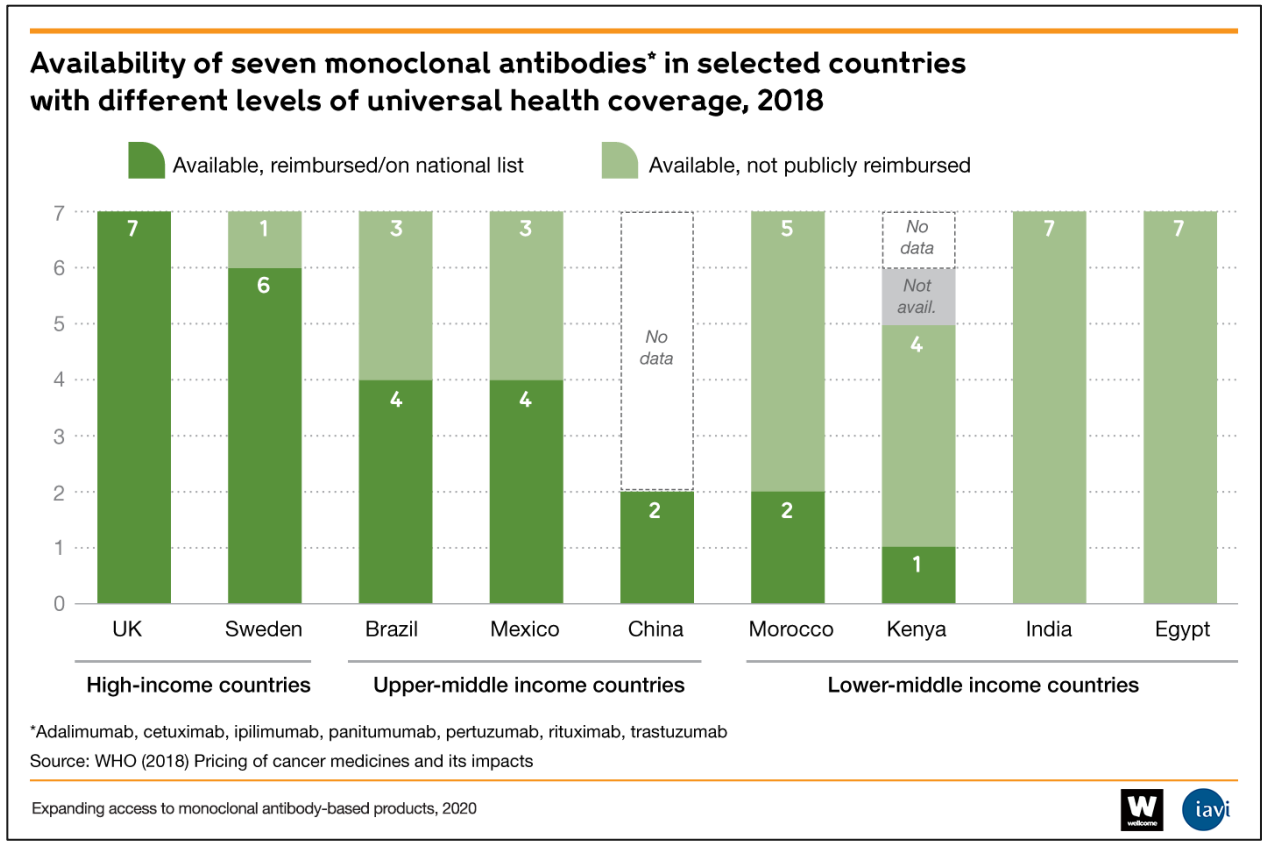
~ 15-20% of the registered mAbs are Biosimilars

Majority of registered mAbs in India are biosimilars

Antibodies are unaffordable and not available in most Public Health Systems in LMICs

availability
+ affordability
= access





- **Antibody US prices (retail) range from $15K – $150K/year**
- **Most commonly prescribed antibodies for NCDs are not reimbursed by LMIC public health systems**

Availability of Antibodies is Severely Limited in LMICs

availability
+ affordability
= access

Barriers:

- Unclear market size and disease burden deterrent to product developers to register in LMICs
- Regulatory processes unclear and capabilities limited - delays in approvals of mAbs ranging from 2-15 years in LMICs
- Collaborative regulatory approaches between stringent and LMIC regulatory agencies and the WHO – so far, used only for small molecules and vaccines
- Limited awareness of the health and economic benefit of mAbs in LMICs – regulators, policy makers, health-care providers, patients

Regulatory approval dates for monoclonal antibodies

Country	Herceptin® (trastuzumab)	Enbrel® (etanercept)	Humira® (adalimumab)	Keytruda® (pembrolizumab)
US	1998	1998	2002	2014
EU	2000	2000	2003	2015
Brazil	1999	2003	2003	2016
China	2002	2010	2011	2018
Egypt	2002	No data	2010	2016
India	2000	2002	No data	2016
Mexico	No data	2001	No data	2016
South Africa	2001	2004	2006	2017
Zimbabwe	2014	Not registered	Not registered	Not registered

Source: IAVI registration analysis

Expanding access to monoclonal antibody-based products, 2020

Emerging WHO specific guidelines and procedures for mAbs: Impact on future availability in LMICs

availability
+ affordability
= access

- WHO disease-specific guidelines for product developers – recently initiated for some infectious disease mAbs
- 6 of 9 Mabs on WHO essential medicine list added in 2019 and LMICs not regularly updating national medicine lists
- WHO prequalification procedures to support UN agency led procurement of mAbs piloted for biosimilars, and are being established for infectious disease mAbs

Figure 7: Monoclonal antibodies included in the WHO Model List of Essential Medicines

Antibody	Brand name	First approved indication	WHO EML inclusion year
Adalimumab	Humira®	Rheumatoid arthritis	2019
Certolizumab pegol	Cimzia®	Crohn's disease	2019
Golimumab	Simponi®	Rheumatoid and psoriatic arthritis, ankylosing spondylitis	2019
Infliximab	Remicade®	Crohn's disease	2019
Nivolumab	Opdivo®	Melanoma, non-small cell lung cancer	2019
Pembrolizumab	Keytruda®	Melanoma	2019
Rituximab	MabThera® Rituxan®	Non-Hodgkin's lymphoma	2015
Trastuzumab	Herceptin®	Breast cancer	2015
Bevacizumab	Avastin®	Colorectal cancer*	2013

*WHO EML for age-related macular degeneration, not licensed for this use. Source: WHO (2019) Model List of Essential Medicines

Competition from Biosimilars, and Second Brands – *when available*, can lower antibody prices and improve access, but not sufficiently

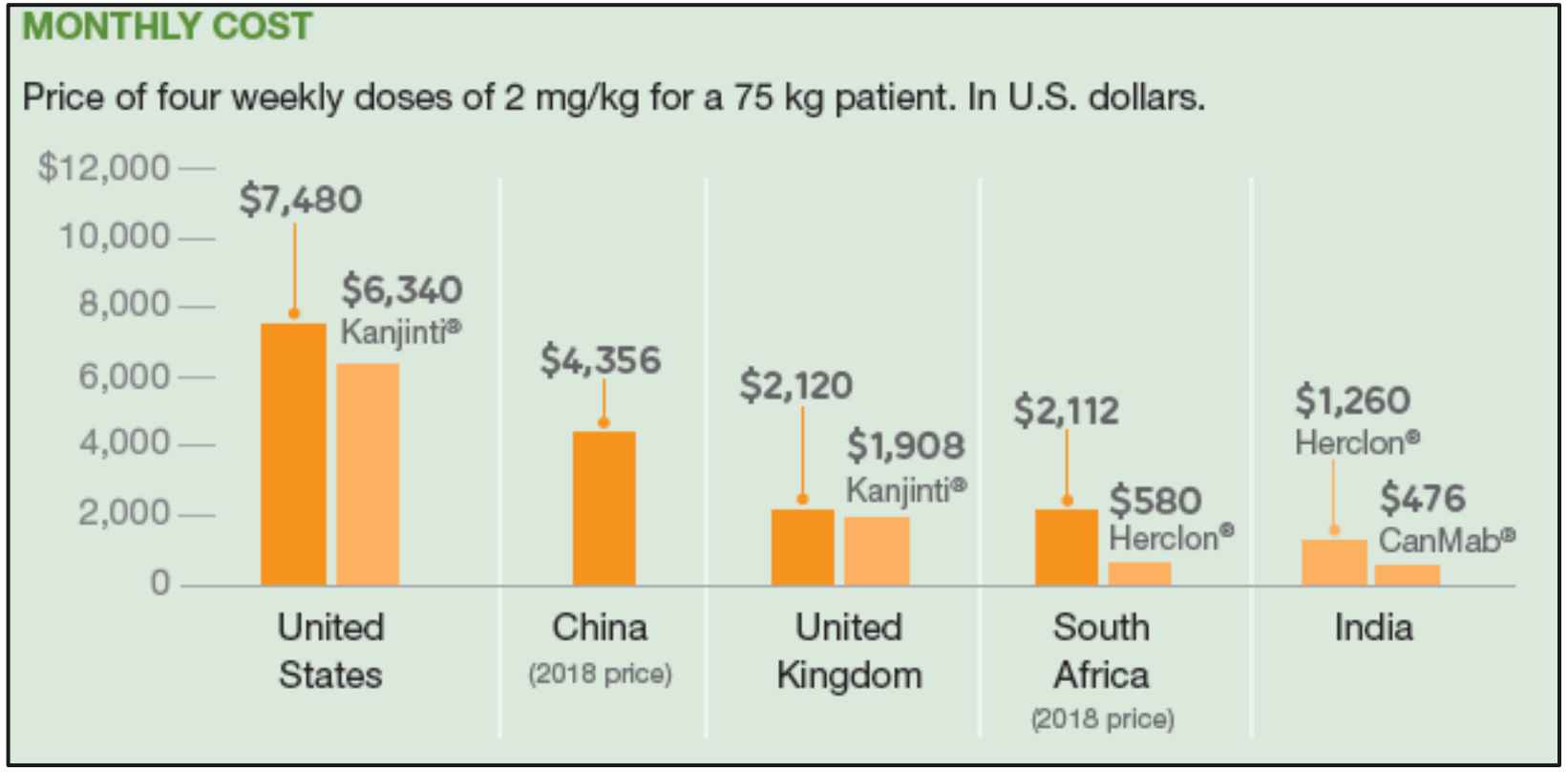
availability
+ affordability
= access

Herceptin® (trastuzumab, for breast cancer) prices:

impact of Biosimilars (Kanjiti®, CanMab®) and Second Brands (Herclon)

BIOSIMILARS

- Similar, but not identical copies of originator mAb and more complex to develop
- 50–100 times more expensive to develop and manufacture than a small molecule generic
- Takes eight to ten years to develop compared to only three to five years for generics[1]

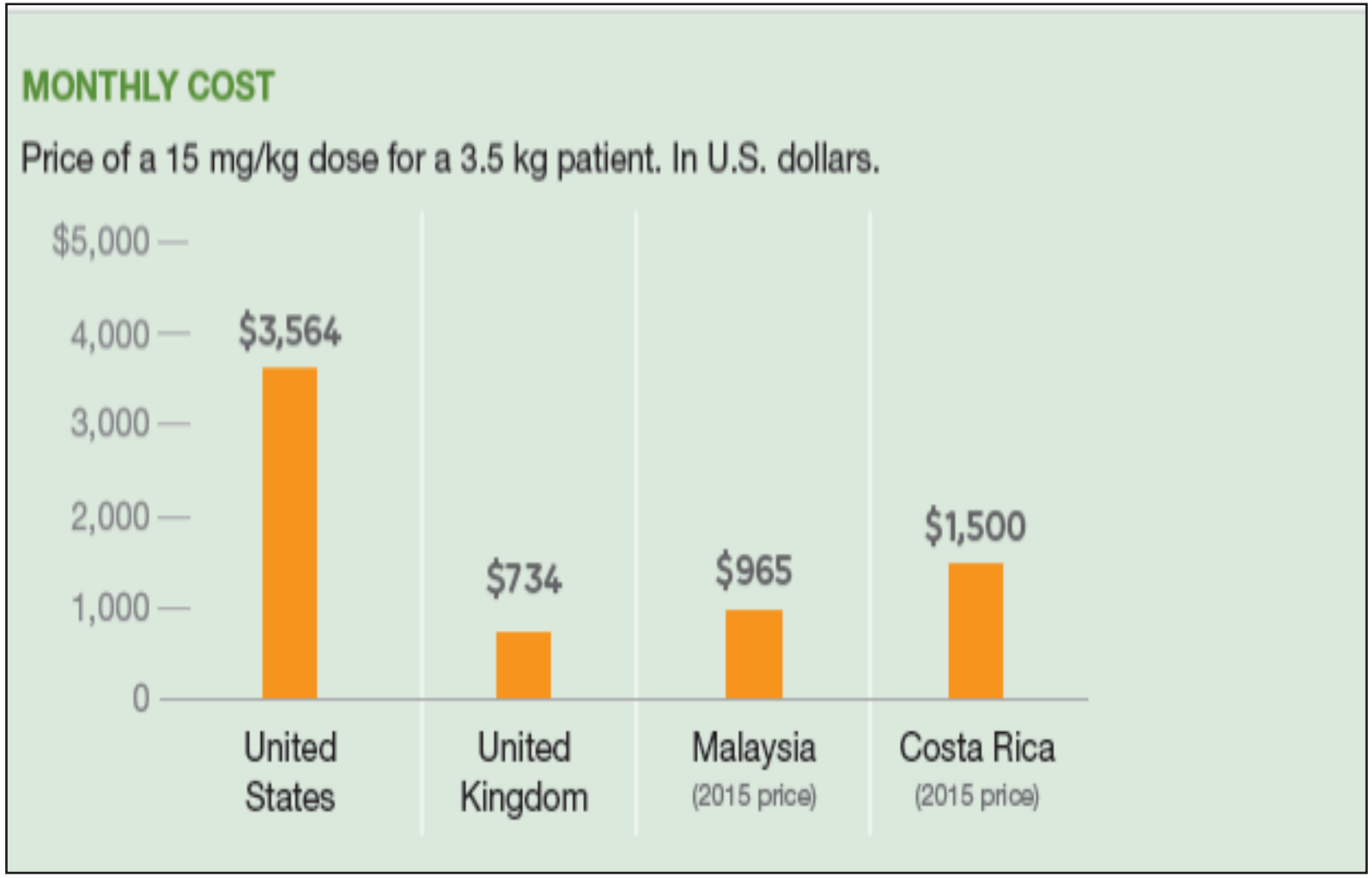


Synagis® : mAb for Prevention of Respiratory Syncytial Viral Infections

Barriers to Access are Affordability and Availability

availability
+ affordability
= access

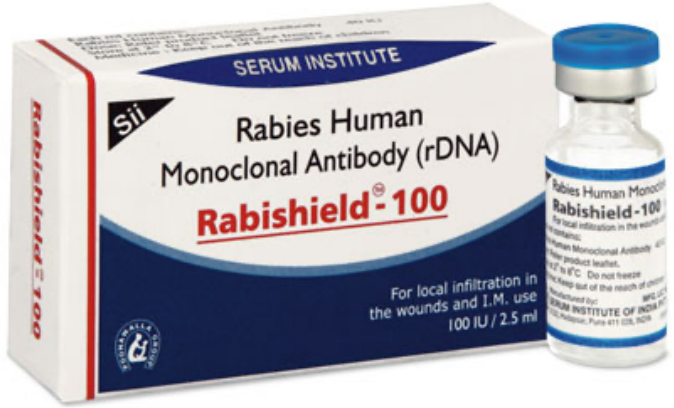
- FDA approval in 1998, global access severely limited
- ***99% of sales in US and Europe***
- ***99% of RSV deaths occur in LMICs!***
- Not included on National medicine lists
- No biosimilars available
- **Next generation long-acting anti-RSV mAbs in late-stage development**



Lower Priced Monoclonal Antibodies are Possible

availability
+ affordability
= access

Rabishield® (Serum Institute of India) and Twinrab® (Zydus Cadilla) for post-exposure prophylaxis of Rabies priced at *$20-40/dose*



$20

RABISHIELD
Company: Serum Institute of India
Indication: Rabies
Dose: 3.3 IU/kg (approx. 0.2 mg/kg)

Critical enablers of low-price include:

- low-dose product
- Regional, low-cost manufacturing
- Lower profit margin business model

Technology Advancements to LOWER the cost of producing and delivering mAbs

availability
+ affordability
= access

- Novel technologies to rapidly isolate and engineer potent antibodies – promise lower dose and cost of production

- Improved biomanufacturing processes in mammalian systems - including single-use reactors, continuous processing, miniaturized, mobile/benchtop bioreactors, facilities with smaller footprints can reduce cost and increase flexibility

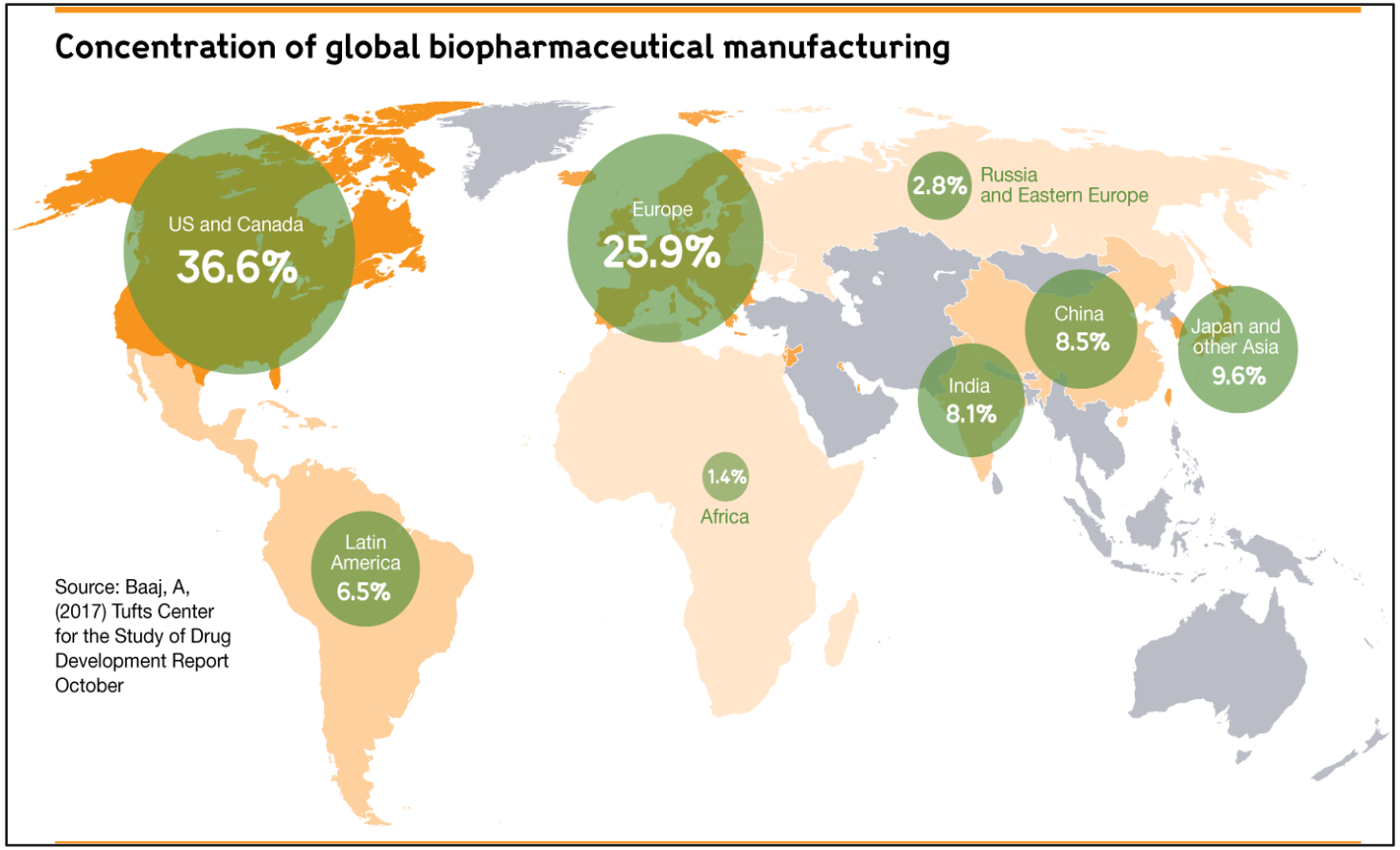
- Alternate production platforms (yeast, fungus, algae, plants) and delivery systems (RNA/DNA, oral) may improve development times and reduce production costs

- Packaging and delivery devices that minimizes cold-chain requirements and improves the patient experience could enhance uptake and lower delivery costs

Biopharmaceutical Manufacturing Capabilities – growing presence in Asia and Latin America

availability
+ affordability
= access

- Majority of biopharmaceutical manufacturing (> 60%) in North America and Europe
- Unclear Market sizes in LMICs a deterrent to investment in expensive facilities
- Local biomanufacturing in Africa severely limited
- Growing presence in Asia and Latin America
- Supply to meet global demand (e.g. for COVID-19) – opportunity to leverage growing presence of facilities in some MICs



Innovative Public-Private alliances for Global Access: Will mAbs for COVID-19 lead the way?

availability
+ affordability
= access

- **Eli Lilly and Bill & Melinda Gates Foundation, as part of the COVID-19 Therapeutics Accelerator, partner on global access to SARS-CoV-2 mAbs**
  - Collaborators AbCellera, Shanghai Junshi, and Columbia University waived royalties for LMICs
  - Commercial manufacturing of SARS-CoV-2 mAbs: at the ***FUJIFILM Diosynth Biotechnologies***

- **IAVI and Scripps Research, MerckKgA and the Serum Institute of India, partner on global access to SARS-CoV-2 mAbs**
  - IAVI/Scripps – antibody discovery and development experience
  - Commercial manufacturing - ***MerckKgA*** in high-income countries, ***Serum Institute of India*** in low- and middle-income countries

A GLOBAL CALL TO ACTION:

Four Parallel Pathways to Expand Access to Monoclonal Antibodies

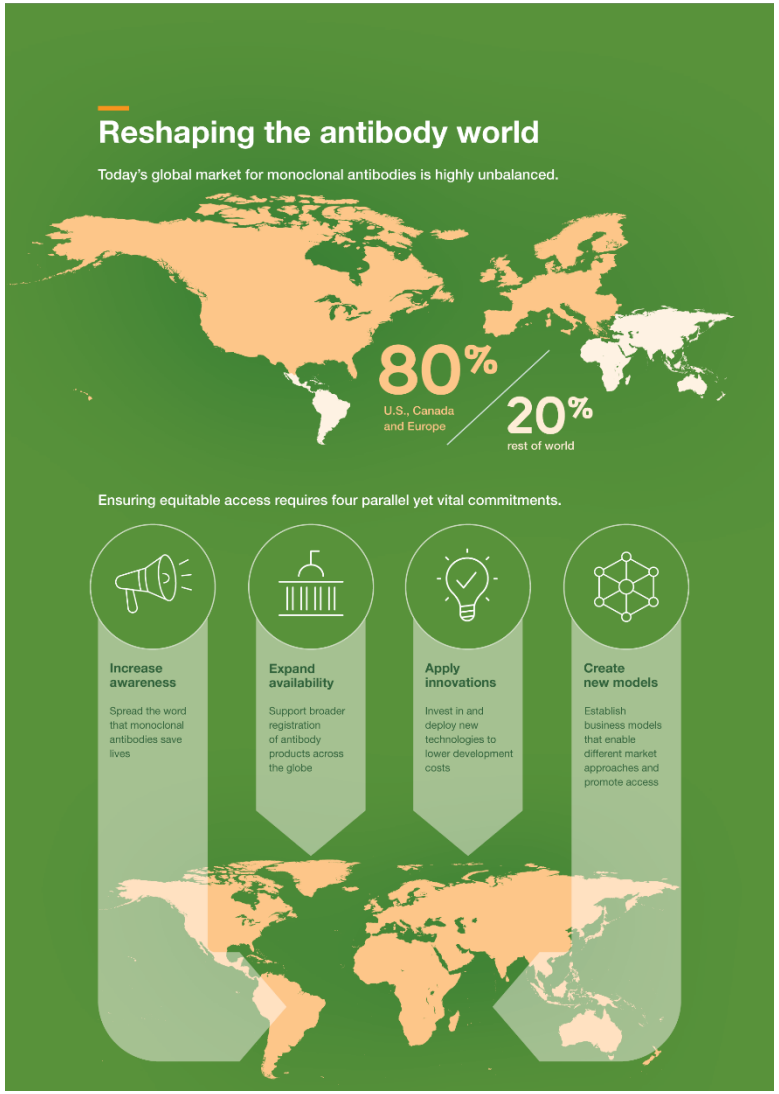
availability
+ affordability
= access

Report outlines specific recommendations and a proposed roadmap for each of the four pathways

CALL to ACTION is relevant to the GLOBAL COVID-19 pandemic response and to enable access to mAbs for all diseases

Report outlines four pathways to promote equitable access to monoclonal antibodies

- **Advocacy** - Monoclonal antibodies save lives: spread the word
- **Policy/regulatory** - Support broader registration and global availability
- **Innovation** - Invest in and deploy innovative technologies to lower the cost of development, manufacturing and delivery
- **Business Models** - Expand and create different partnership and market approaches in low-, middle- and high-income countries



Global Access through implementation of priority actions

availability + affordability = access

availability

ADVOCACY

- **Increase awareness at all levels** – governments, MOAs, Health technology assessment groups, patients, health-care providers, on the clinical/public health value
- Conduct studies to **model the health and economic impact** of introducing mAbs in LMICs
- Convene **key opinion leader meetings**

POLICY AND REGULATORY

- Product developers/WHO collaborate to develop **disease-specific guidelines** for mAbs
- Harmonize, expand and use **collaborative registration pathways** to enable accelerated registrations and ultimately access in LMICs
- Expand inclusion of mAbs into national and WHO **essential medicine lists**

Global Access through implementation of priority actions

availability
+ affordability
= access

+ affordability

INNOVATION

- Ensure that technological advancements that enable global access are **integrated early into product development**
- **Test new technologies and platforms** (including those applied to lower priced biosimilars) that have the potential to lower costs

BUSINESS MODELS

- Expand existing but limited industry-led **patient access plans** by strengthening health systems
- Expand **global pricing frameworks**
- Identify **donor-funded procurement** bodies
- Explore **alternate manufacturing and supply chains** in different regions that enable market differentiation and provision of more affordable mAbs in LMICs
- Identify creative solutions to manage **intellectual property**

Raising support and accelerating action for mAb access

availability
+ affordability
= access

- Launch of the IAVI-Wellcome Call to Action - supported by key opinion leader quotations, social media outreach, interviews, news reports, is **raising awareness of the inequity of access to mAbs across a spectrum of stakeholders and geographies**

- **Virtual webinars/KoL events** are planned with partners across multiple geographies and disease areas

- IAVI, through its HIV and SARS-CoV-2 mAb programs, is leading the **implementation of some priority actions for global access**

Key Strategic Objectives

1. ***Increase awareness of the major inequity in access*** to affordable antibodies and secure support of key opinion leaders for the calls to action
2. ***Achieve buy-in from the Global Health community*** to engage in and collaborate on the calls to action
3. ***Drive change through implementation*** of priority actions

Key Opinion Leader reactions to IAVI-Wellcome Publication

> Monoclonal antibodies are a highly promising technology that have not yet realized their potential in lower-income settings, largely due to price and scale. WHO therefore welcomes all efforts from partners that increase global access to high quality, safe and effective monoclonal antibody products, for COVID and other diseases.

Soumya Swaminathan, M.D., M.B.B.S.
Chief Scientist, World Health Organization

> Bringing together the very brightest minds from across all sectors will help ensure that life-saving innovations will be made available affordably and at scale to all that need them. The Call to Action by IAVI and Wellcome on expanding access to monoclonal antibody-based products represents a critical first step on the journey to achieve this goal.

Peter Piot, M.D., Ph.D.
Director of the London School of Hygiene & Tropical Medicine

> In the midst of a pandemic, it is imperative for leaders across the globe to stand strong behind the call to action by IAVI and Wellcome to realize a roadmap global access to innovative antibody-based soluti for COVID-19 and other diseases.

Eric Goosby, M.D.
Director, Center for Implementation Sciences, Global Health Scien at the University of California, San Francisco, and IAVI Board Chair

> This report is a timely effort by Wellcome and IAVI and will help funding agencies and researchers globally to understand the gaps and provide solutions to address them.

Renu Swarup, Ph.D.
Secretary, Department of Biotechnology, Ministry of Science and Technology, Government of India; Chairperson, BIRAC

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