Clinical Trial Site Selection and Strategy

2025 GILEAD PHARMA CASE COMPETITION

Michael Calcagno, Armaan Kamdar,
Rebecca Zhang, and Alvin Zhu

GILEAD SCIENCES, INC | 2025

GILEAD
Creating Possible

Table of Contents

Disclaimer

This case was prepared by Michael Calcagno, Armaan Kamdar, Rebecca Zhang, and Alvin Zhu solely as the basis for discussion, with support from several others at Gilead across departments and functions.

The assumptions and simplifications made in the case allow for uniform understanding of the materials across teams. Although this case is based largely on actual procedures and initiatives, the case materials should not be considered a complete summary, endorsement, or projection of any action taken or to be taken by Gilead Sciences. The scenario presented in this case was designed based on research conducted in the public domain and creatively altered to meet the guidelines of this academic competition and learning exercise. It does not reflect any coordination with Gilead Sciences, or proprietary knowledge of its product pipeline. In addition, this case does not represent the official views of the authors.

These materials can only be used for the **2025 Gilead Pharma Case Competition**.

Executive Summary

Since his appointment in 2014, MARA Therapeutics CEO Steven A. Skiff has spearheaded the company's strategic expansion into new therapeutic areas, with a particular focus on infectious diseases (ID). Under his leadership, the Development organization has launched research & development (R&D) targeting multidrug-resistant tuberculosis (MDR-TB), aligning corporate growth with a broader mission to deliver effective and globally accessible treatments.

Ramafloxacin, originally approved in 2002 for community-acquired pneumonia and later expanded to include treatment of skin and soft tissue infections, is now positioned for a new indication: MDR-TB. Currently undergoing Phase II with promising data emerging, the Development Leadership Team (Dev LT) is eager to initiate planning for the upcoming Phase III ramafloxacin trial.

As part of this effort, Dev LT is evaluating potential sites across North America, Asia and Africa. Your team has been tasked with evaluating and prioritizing sites in Africa, taking into consideration both operational logistics for trial execution, as well as strategic implications for post-approval commercialization.

Dev LT expects your team to provide a series of strategic recommendations that includes a projected trial timeline, prioritization and selection of sites, risk mitigation strategies, and estimated treatable patient population for ramafloxacin. For Skiff's full directive, see *Case Competition: Key Questions and Considerations*.

About MARA Therapeutics

Company Overview

MARA Therapeutics was founded in 1987 in Boston, Massachusetts by Tay Jatum and Alex Wojnowski, former colleagues at BMP Pharmaceuticals. From the outset, their mission was to deliver innovative therapies to patients worldwide, focusing on infectious diseases that disproportionately affect vulnerable populations and lack effective treatment options. To advance this vision, they appointed Dr. K.G. Pierce as Chief Medical Officer (CMO), who led the development of therapies for human immunodeficiency virus (HIV) and respiratory tract infections.

While MARA initially concentrated its efforts on HIV, the company shifted its focus over the past decade to tuberculosis (TB), driven by the persistently high incidence rates in low- and middle-income countries (LMICs).

Following Wojnowski's retirement in 2012, Jatum assumed the role of sole Chairman. Steven A. Skiff was brought on as Chief Executive Officer (CEO), bringing expertise from Silver-Stern Medical Group, where he specialized in clinical study planning across East Asia. Skiff introduced a renewed strategic direction, emphasizing the development of treatments that not only reduce infectious disease burden but also advance global health equity in underserved areas. Skiff championed similar initiatives during his prior work with the West-Russell Foundation, a nonprofit organization where he helped establish several community-based HIV treatment clinics throughout West Africa.

Since its public listing in 2004, MARA Therapeutics has grown from a modest operation of approximately 800 employees to a global workforce exceeding 6,000 employees. The company has expanded its presence to five countries: the United States, Germany, China, Ireland, and Singapore. Its headquarters remain in Boston, with additional offices in South San Francisco, San Diego, and Chicago. Regional hubs in Singapore and Ireland support strategic partnerships across Europe and Asia, while mid-sized manufacturing facilities in Munich and Shanghai bolster production capabilities.

Company Mission

MARA Therapeutics has long been guided by a corporate ethos rooted in **innovation**, **authenticity** and **community**. The company's mission is to deliver equitable and

accessible treatments that contribute to a healthier world for all. In pursuit of this goal, MARA has consistently prioritized corporate citizenship as a core component of its operations.

Key Personnel & Organizational Structure

In preparation for the upcoming Phase III ramafloxacin trial, Dr. K.G. Pierce has brought **Kasey Durant** onboard as **Senior Vice President (SVP) in Clinical Development**. Durant brings extensive experience in clinical research across Africa and Asia, having planned and executed trials in countries including South Africa, Nigeria and Egypt. Durant's academic collaborations with hospitals and universities in these regions and familiarity with local regulatory agencies serve as a strategic asset for global trial execution.

Durant will work closely with other Dev LT members and will provide executive leadership and oversee the study teams assembled specifically for this trial. For more details on the company's organizational structure, see *Exhibit C: Organization Chart*.

Portfolio Overview

MARA Therapeutics began its drug development efforts in the antiretroviral space during the height of the HIV epidemic. The company's first breakthrough came in 1995 with FDA approval of gilentolimod (LooMey). As competing pharmaceutical companies intensified their focus on antivirals, the market became increasingly saturated. In response, MARA strategically broadened its R&D pipeline towards additional indications in the infectious disease space, with a particular focus on antimicrobial resistance. This shift ultimately led to the approval and launch of ramafloxacin in 2002. Since then, MARA has broadened its infectious disease portfolio, with a growing emphasis on tuberculosis.

Currently, MARA has a series of ongoing clinical trials at various stages: 11 in Phase I, 7 in Phase II, and 4 in Phase III. The company remains committed to advancing research in infectious disease and virology. For more details, see *Exhibit D: Pipeline*.

RESI Phase III Trial

Ramafloxacin is a small molecule drug structured similarly to fluoroquinolone antibiotics, with a novel and targeted mechanism of action. Originally developed as an intravenous (IV) solution for earlier indications, MARA scientists have reformulated it into a once-daily oral tablet for investigation in the treatment of MDR-TB.

The drug is currently undergoing a Phase II noninferiority trial, demonstrating positive safety and efficacy data compared to the standard of care MDR-TB regimen containing moxifloxacin, the traditional fluoroquinolone-based agent.[1] Ramafloxacin is showing early indications of potential clinical benefit and reduction in overall treatment duration.

Encouraged by positive readouts, LT has initiated planning for the upcoming **Phase III RESI trial**, with a strategic focus on accelerating time-to-market to address unmet medical needs and improve standards of care. MARA has allocated a substantial budget for the trial and is prepared to increase investment to outpace competitors pursuing similar indications. The End-of-Phase II meeting is expected to occur in Q2 2026.[2]

The **RESI trial protocol** has been designed to ensure consistent monitoring of safety and efficacy while supporting adherence and optimizing patient outcomes. Below is a high-level summary of key details:

Approximately 80% of screened candidates diagnosed with MDR-TB are expected to meet the eligibility criteria for enrollment in the RESI trial. Screening will involve a series of diagnostic assessments, including sputum culture testing, drug susceptibility testing, and chest X-rays, all of which require specialized laboratory equipment and trained personnel. Participants who qualify will receive a 30-day supply of ramafloxacin at each monthly visit, alongside routine clinical evaluations and laboratory testing. Treatment will continue until a favorable outcome is achieved (defined as two consecutive monthly visits with negative culture results) or a maximum treatment duration of 40 weeks, whichever occurs first.

In close alignment with ICH E17 principles[3], MARA is prioritizing new relations and expanding its global clinical trial footprint to include LMICs in Africa. The goal is to identify diverse trial sites to support a patient enrollment target of 300 to 500 participants. Existing clinical trial sites for the multiregional RESI trial have already been established by MARA's global clinical operations teams in Europe and Southeast Asia.

Clinical Trial Background

Tuberculosis Overview

Tuberculosis (TB) is a highly infectious disease transmitted through the respiratory system, primarily affecting the lungs. Since 2023, TB has remained the world's leading cause of death from a single infectious agent. Each year, approximately 10.8 million people contract TB globally, resulting in 1.25 million deaths. Notably, nearly 80% of cases and deaths occur in LMICs, indicative of disparities in healthcare access and the broader impact of social determinants of health. Recognizing its global burden, TB has been designated a priority by

[1] "Treatment for Drug-Resistant Tuberculosis Disease," Centers for Disease Control and Prevention
[2] "The Crucial End of Phase 2 FDA Meeting: A Drug Development Milestone," Bracken
[3] "ICH Guideline E17 on general principles for planning and design of multi-regional clinical trials," EMA

the United Nations Sustainable Development Goals (SDGs), with the objective of ending the TB epidemic by 2030.[4]

The graphic below shows the estimated TB incidence rate by country (World Health Organization):[5]

The standard treatment regimen for TB consists of a four-drug combination administered over 6 months. A newer rifapentine-based regimen, approved in 2025, has reduced this duration to 4 months.[6] However, even these shortened regimens pose challenges: long treatment duration often leads to non-adherence and mismanagement, and ultimately, drug resistance. Resistance can also arise from other causes such as inappropriate medication use, ineffective formulations, premature treatment interruption, and direct transmission of resistant strains.

Multidrug-resistant tuberculosis (MDR-TB) is a form of TB disease that is resistant to the standard treatment regimen. In 2002, an estimated 410,000 people developed MDR-TB. Treatment success rates remain significantly lower compared to drug-sensitive TB, largely due to the complexity and duration of MDR-TB regimens. While the global treatment success rate improved from 50% in 2012 to 63% in 2020, substantial progress is still needed.

[4] "Tuberculosis (TB)," World Health Organization
[5] "1.1 TB Incidence," World Health Organization
[6] "TB Disease Treatment: 6- or 9-Month Ripe TB Treatment Regimen," Centers for Disease Control and Prevention

Further, access to care remains a critical barrier. In 2023, only 2 in 5 patients with drug-resistant TB were able to access appropriate treatment. Current treatment regimens are often individualized, and the unmet medical need for more effective and accessible therapies remains high.[7] While community engagement is a critical component in managing most disease states, its role is comparatively limited in MDR-TB. Instead, timely screening for drug resistance and prioritizing access to effective treatment options are more impactful in improving outcomes.

Site Selection

The **site selection process** is a major determinant of clinical trial success as it directly impacts patient safety, data quality, and trial timelines. While each site is evaluated on an individual basis, 6 key categories may guide the selection process:[8]

1. **Patient-Related Factors:**
   - Availability of eligible patients within the site's accessible area
   - Representation across target patient demographics

2. **Site & Investigator Experience:**
   - Reputation and history of high data quality and compliance
   - Qualifications and experience in conducting clinical studies

3. **Regulatory & Ethical Environment:**
   - Presence and maturity of national regulatory authorities
   - Requirements for local data or bridging studies for regulatory submissions

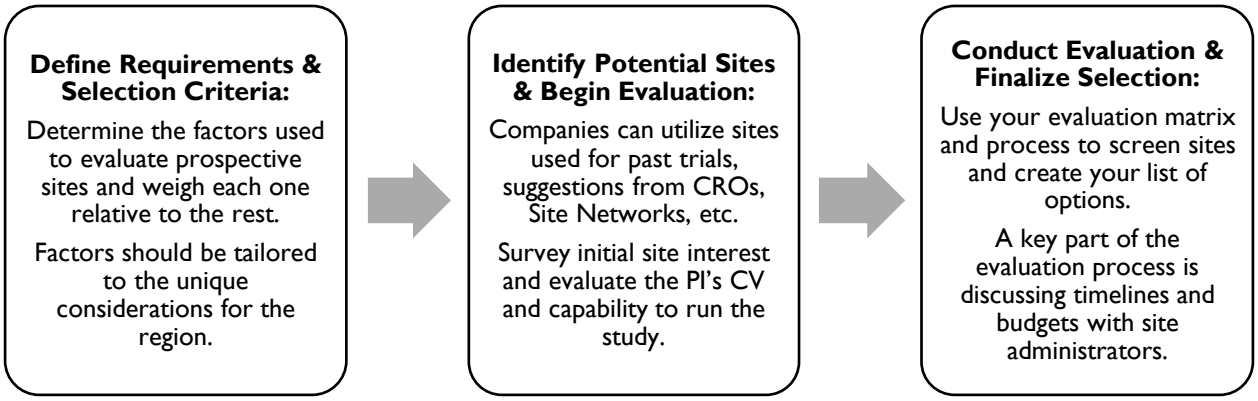
4. **Operational & Infrastructure Capacity:**
   - Availability and quality of facilities (e.g., labs, cold storage)
   - Site adherence to Good Clinical Practice (GCP) and infrastructure standards

5. **Logistics & Geography:**
   - Accessibility of the site for patients and staff
   - Ease of transportation of materials and communication to global teams

6. **Competitive Trial Environment:**
   - Presence of competing trials in similar therapeutic areas
   - Site capacity to manage multiple concurrent studies

[7] "Tuberculosis: Multidrug-Resistant (MDR-TB) or Rifampicin-Resistant TB (RR-TB)," World Health Organization
[8] "The Ultimate Guide to Site Selection for Clinical Trials," Lindus Health

The current standard for site selection is a systematic, three-step process[9]:



Selecting high-quality sites that align with protocol requirements will more likely result in faster timelines for activation, efficient patient recruitment, and higher data quality. Conversely, poor site selection increases the risk of delays, by up to 30%, and can significantly impact trial costs.[10] Beyond the operational setbacks, delays in product approvals and launches can cost companies several million per day.[11]

Timeline Projections

Establishing and adhering to a clear timeline is essential for trial efficiency. Key milestones typically include ethics approval and site activation dates; patient recruitment and enrollment targets e.g., First Patient In (FPI), Last Patient In (LPI); database lock; and planned regulatory submission and approval dates.

Once sites are selected, the next phase is site activation. Each site goes through an initiation process involving GCP and protocol training, contracting, submission and approval of all required GCP documents, and ethics committee approval. Timely execution of these steps ensures smooth trial progression and supports regulatory success.[12]

While rapid enrollment is critical to meeting trial timelines, equal emphasis must also be placed on patient retention throughout the study. High dropout rates can compromise data integrity, delay key milestones, and ultimately impact trial outcomes. To mitigate these risks, proactive strategies such as patient engagement plans, regular site communication, and close monitoring of retention metrics should be integrated into the timeline to ensure trial continuity and success.

[9] Anais Silva, "Selecting Study-Appropriate Clinical Sites in 3 Steps," Applied Clinical Trials
[10] "Optimizing Site Selection and Management for Clinical Trial Success," Pulse
[11] "Optimizing Your Clinical to Commercial Journey," PCI Pharma Services
[12] "Maximizing Efficiency in Clinical Trial Timelines," Lindus Health

Ethics Committees

Ethics Committees (EC) are an integral part of the pharmaceutical regulatory framework in many countries. Often affiliated with specific healthcare institutions or regional authorities, ECs are responsible for reviewing and approving study protocols, ensuring patient safety and rights, and monitoring compliance throughout the trial.[13] If a study is found to be insufficient in any of these areas, ECs can either mandate modifications or reject proposals outright.

In Africa, ECs face increasing complexity due to high disease prevalence, large patient populations, and greater variability in infrastructure quality and staff experience. As more trials are conducted across the continent, the role of ECs becomes even more critical in safeguarding ethical standards and ensuring patient safety and trial integrity.

Pharmaceutical Landscape in Africa

Low- and Middle-Income Countries

Low- and middle-income countries (LMICs) are classified by the World Bank based on gross national income per capita, identifying lower average socioeconomic status.[14] Within the healthcare sector, this designation underscores the need to reduce health disparities across nations. LMICs often face systemic challenges such as underdeveloped healthcare systems, higher mortality rates, and limited access to medical services. Addressing these disparities is essential to improving global health outcomes and advancing health equity.

While there has been a recent uptrend in the number of clinical trials conducted in LMICs, the overall representation remains disproportionately low. According to the World Health Organization, only 32% of randomized clinical trials occur in 113 LMICs, despite these countries comprising over 75% of the global population. Pharmaceutical companies are increasingly interested in conducting trials in LMICs, driven by regulatory guidance recommending greater trial diversity and the presence of untreated patient populations. However, several challenges persist, including limited research infrastructure, complex ethical considerations, and variability in local regulatory and health authority support.[15] These factors must be carefully evaluated when planning clinical trials in LMICs to ensure feasibility, compliance, and ethical integrity.

Africa Landscape Overview

Despite historically high rates of infectious disease and chronic diseases like diabetes, hypertension, and cardiovascular conditions, the pharmaceutical sector in Africa remains relatively nascent. Most countries rely heavily on imports primarily from Asia, as well as

[13] "Ethics Committees: Structure, Roles, and Issues," Journal of Korean Medical Science
[14] "World Bank Country Classifications by Income Level for 2024-2025," World Bank Blogs
[15] "Trials and Tribulations: Running Clinical Trials in Lmics Can Be a Challenge," ASH Clinical News

North America and Europe. Even in nations with emerging pharmaceutical industries, active pharmaceutical ingredients (APIs) and other key components are often imported, creating vulnerabilities in supply chains and limiting scalability.

To help navigate new countries, pharmaceutical sponsors often rely on Contract Research Organizations (CROs) to serve as intermediaries with clinical trial sites, ethics committees, and national health authorities. CROs can play a critical role in ensuring regulatory compliance and maintaining consistent communications across key stakeholders. However, identifying a CRO with a strong footprint and operational fluency across multiple countries can be challenging. Sponsors must carefully evaluate CRO capabilities and regional expertise to ensure successful trial implementation.

Country-Specific Background

The countries selected for potential trial sites (*See Exhibit I: Potential Clinical Sites in Africa)* were chosen based on their established domestic pharmaceutical industry relative to the rest of Africa. While each presents unique strengths and limitations, all offer viable opportunities for MARA Therapeutics to conduct its Phase III trial. In evaluating these opportunities, it's important to consider that local trial requirements vary by country, and trial site selection does not always directly correlate with filing or commercialization plans. Each market must be assessed individually to ensure alignment with clinical, regulatory and commercial objectives.

Below is a summary of each country's pharmaceutical landscape, regulatory environment, and ethics committee infrastructure.

Egypt

Egypt's pharmaceutical industry is among the more robust in Africa, with an expected **total revenue of $1.59 billion USD in 2025**.[16] The projected **compound annual growth rate (CAGR) through 2030 is 6.45%**, which indicates that the sector is positioned to grow for the rest of the decade.[17] Most pharmaceutical companies are located in **Cairo**, **Giza** and **Alexandria**, where infrastructure is advanced and skilled personnel are available.

Domestic production accounts for 91% of all drug sales in the country, with oncology treatments comprising the bulk of imports.[18] High population demand for affordable medications is driving the effort to expand pharmaceutical manufacturing, and increased investment into biopharmaceutical research. This is supported by government initiatives such as public-private partnerships and fiscal incentives to boost exports.[19] However, recent medication shortages, largely due to foreign currency constraints affecting the

[16] "Pharmaceuticals - Egypt: Statista Market Forecast," Statista
[17] "Egypt Pharmaceutical Market 2024-2030," Mobility Foresights
[18] "Egypt's Health Minister Discusses Challenges and Achievements in the Pharmaceutical Sector"
[19] "Economic Pressures Strain Egypt's Pharmaceutical Sector amid Efforts for Stabilization and Growth"

import of raw materials, highlight a strategic vulnerability. Despite strong domestic production, reliance on imported components poses risks to supply chain stability.[20]

The two principal regulatory authorities in Egypt are the Ministry of Health & Population (MHP) and the Egyptian Drug Authority (EDA). The MHP is responsible for overseeing national health policy and public health compliance. The EDA operates under the MHP and is responsible for drug registration and approval, clinical trial oversight, manufacturing standards, and pharmacovigilance for approved medications.[21]

ECs in Egypt are attached to institutions and are often referred to as Institutional Review Boards (IRBs). The Egyptian Network of Research ECs (ENREC) coordinates review policies and practices across over 50 IRBs in Egypt, promoting consistency and quality.[22] These IRBs are governed by MHP guidelines and international standards such as GCP.

Ethiopia

Ethiopia's pharmaceutical industry is one of the fastest growing in Africa, with a focus on generic drug production. The industry is projected to reach **$426 million USD in total revenue in 2025, with a CAGR of 3.2% through 2030**.[23] Most companies are based in **Addis Ababa**, due to the availability of government support and infrastructure.

Approximately 85% of pharmaceuticals used in Ethiopia are imported and domestic production remains limited.[24] The government has taken steps to boost the industry, with the Ethiopian Pharmaceutical Supply Agency (EPSA) providing a 25% price protection for local manufacturers, as well as various infrastructure investments including the Kilinto Industrial Park, a GMP-compliant facility designed to support pharmaceutical manufacturing. However, despite these efforts, a recent industry survey revealed concerns on underutilized resources, weak R&D capacity, and persistent barriers to export. Operational instability and infrastructure constraints continue to hinder growth, suggesting that while potential exists, robust support systems are still developing.[25]

The agencies overseeing the pharmaceutical sector in Ethiopia are the EPSA, Ethiopian Food and Drug Authority (EFDA), and the Food, Medicine & Healthcare Administration and Control Authority (FMHACA), responsible for product registration, licensing and inspection. Recent regulatory harmonization efforts across agencies have improved clarity, and while

[20] "Egypt's Battle against Medicine Shortages," Egypt Business Directory
[21] "An Overview of Pharmaceutical Regulations in Egypt," Generis Global Legal Services
[22] "Ethical Analysis of Egypt's Law Regulating Clinical Research"
[23] "Pharmaceuticals - Ethiopia: Statista Market Forecast," Statista
[24] "Trends and Challenges in Access to Essential Medicines in Ethiopia and the Contributions of Local Pharmaceutical Production"
[25] "Challenges Hinder Growth of Ethiopia's Pharmaceutical Sector," Market Access Today

challenges remain, the regulatory environment in Ethiopia is strong and well-regarded internationally.[26]

ECs in Ethiopia are relatively new compared to other countries, with most concentrated in Addis Ababa at hospitals and universities. Although ECs have demonstrated understanding of clinical review standards and processes, limited experience has led to delayed timelines and general incoherence across the healthcare system.[27]

Kenya

As the third largest pharmaceutical exporter in Africa, Kenya is well-positioned to play a leading role in the continent's drug development and innovation.[28] The growing population and economy have driven a national interest in bringing pharmaceutical development and manufacturing to domestic sources. High prevalence of various infectious and viral diseases, as well as chronic conditions, has also further accelerated industry growth. Total revenue is expected to reach **$560.15 million USD in 2025**, with a **CAGR of 4.11% through 2030**, indicating strong growth year over year.[29] The industry is heavily concentrated in **Nairobi**, largely due to the government being the primary purchaser of domestically produced medications.

The Universal Health Coverage facilitates nationwide distribution of medications, supporting both public and private sector growth. However, access remains a challenge; 18% of the country does not meet WHO criteria for patient accessibility, primarily due to inadequate healthcare infrastructure.[30]

Pharmaceutical regulatory oversight in Kenya is led by the Pharmacy & Poisons Board (PPB), which governs pharmacy operations and drug registration. Clinical research and development is subject to domestic laws and WHO guidelines, though drug approval timelines (12-24 months) and overlapping, and sometimes conflicting, mandates across agencies present ongoing challenges.[31]

In Kenya, local ECs are institution-based and must be accredited by the National Commission for Science, Technology & Innovation (NACOSTI) before evaluating and approving clinical trials. These committees evaluate proposed studies based on various regulatory and governmental standards.[32]

---

[26] "Understanding Pharmaceutical Regulations in Ethiopia: A Comprehensive Guide," Generis Global Legal Services
[27] "Composition and Capacity of Institutional Review Boards, and Challenges Experienced by Members in Ethics Review Processes in Addis Ababa, Ethiopia: An Exploratory Qualitative Study"
[28] "Kenya Pharmaceutical Market 2024-2030," Mobility Foresights
[29] "Pharmaceuticals - Kenya: Statista Market Forecast," Statista
[30] "Overview of Pharmaceutical Industry in Kenya," Prunus Pharma
[31] "An Overview of Pharmaceutical Regulations in Kenya," Generis Global Legal Services
[32] "Clinical Research Regulation for Kenya," National Institute of Allergy and Infectious Diseases

Morocco

Morocco's pharmaceutical industry is among the most advanced in Africa. Approximately 65-70% of medications used domestically are manufactured locally and about 10% of production is exported.[33] The pharmaceutical sector contributes 5.2% to gross domestic product (GDP), supporting over 55,000 jobs. Industry hubs are primarily located in **Casablanca, Rabat, Tangier and Bouskoura**. Revenue is projected to reach **$683.64 million USD in 2025**, with a **CAGR of 4.99% through 2030**.[34]

Although Morocco is well-established and positioned to grow in the coming years, the industry faces potential weaknesses such as its heavy reliance on imported raw materials and APIs. To mitigate this risk, the government has announced major investments aimed at achieving "health sovereignty." However, global supply chain disruptions remain a significant risk to drug development and production continuity.[35]

The main regulatory body in Morocco is the Pharmacy & Medicines Directorate of the Ministry of Health & Social Protection, with additional alignment to the African Medicines Agency. Morocco's regulatory standards are among the strictest in Africa, and approvals in the country are often recognized by international agencies such as the U.S. FDA and EMA.[36]

Ethics committees in Morocco are region-specific, with 11 across major cities including Rabat, Casablanca, Marrakech, Fez, Tangier and Oujda. These ECs operate under the Ministry's guidelines and are supported by the National Commission for the Protection of Personal Data, which ensures patient privacy is protected during clinical research.[37]

Nigeria

The pharmaceutical industry in Nigeria is experiencing rapid growth, with projected revenues of **$1.84 billion USD in 2025**, and a **CAGR of 6.41% through 2030**.[38] Most pharmaceutical companies are in **Lagos**, with further industry clusters in **Abuja**, **the Central States**, **and the Southwest region**.

Nigeria's large population and high rates of infectious disease make it a critical market. However, domestic production remains insufficient to meet its demand due to reliance on imported materials ($643 million USD value in 2024)[39] and a shortage of skilled personnel within the industry.[40] To address these gaps, the government recently launched the Health Sector Renewal Investment Initiative aimed at improving healthcare affordability and

[33] "Pharmaceutical – An Industry with Global Ambitions," Morocco Now
[34] "Pharmaceuticals - Morocco: Statista Market Forecast," Statista
[35] "Morocco's Pharmaceutical Industry, Second in Africa in Terms of Turnover," Atalayar
[36] "Understanding Pharmaceutical Regulations in Morocco: An in-Depth Analysis," Generis Global Legal Services
[37] "Precision Medicine in Morocco: State of Art and Challenges for Implementation," Journal of Cancer Policy
[38] "Pharmaceuticals - Nigeria: Statista Market Forecast," Statista
[39] "Nigeria Imports of Pharmaceutical Products," Trading Economics
[40] "Pharmaceutical Industries in Nigeria: Challenges and Prospects," Pharmapproach

expanding local drug manufacturing. Overcoming these challenges will be essential for Nigeria to sustain its growth and compete globally.[41]

The National Agency for Food & Drug Administration & Control (NAFDAC) is the primary regulatory body, overseeing drug development and manufacturing. Facilities are subject to NAFDAC inspections to ensure compliance with Good Manufacturing Practices (GMP), WHO guidelines and the Federal Ministry of Health. Additional oversight is provided by the Pharmacists' Council of Nigeria and National Institute for Pharmaceutical R&D.[42]

ECs in Nigeria are institution-based and governed by the National Health Research Ethics Committee (NHREC), which establishes and enforces research review guidelines and approval procedures. Local ECs will focus primarily on oversight of ongoing research activities, while the NHREC holds final approval over all proposed clinical studies.[43]

South Africa

South Africa's pharmaceutical industry is well-developed and maintains a strong international presence. Total revenue is projected to be **$3.47 billion USD in 2025**, with **market volume expected to exceed $4.3 billion by 2030**.[44] Industry activity is concentrated in **Cape Town** and **Durban**, with additional hubs in the Western and Eastern Cape regions.

The country's domestic industry has focused on production of antiretrovirals and received a significant boost during the COVID-19 pandemic through vaccine manufacturing. Ongoing investment from both public and private stakeholders is driving strategic shift towards increased generic drug production and domestic development of new treatments. A key challenge is the wealth disparity across the population, which has resulted in a two-tiered healthcare system. While most citizens rely on government-provided healthcare at lower costs, wealthier individuals can access private healthcare services. This disparity has created barriers to medication accessibility under the current healthcare model.[45]

The main regulatory agency is the South African Health Products Regulatory Authority (SAHPRA), under the National Department of Health. SAHPRA regulates all medicinal products intended for human or animal use, including clinical trials, licensing for manufacturers and retailers, and product distribution throughout the country. SAHPRA has aligned many of its guidelines with those of the WHO, EMA, and U.S. FDA, lending international credibility to its approvals and facilitating export opportunities.[46]

[41] "New Executive Order: Hope for Nigeria's Health Sector amid the Economic Challenges," Nigeria Health Watch
[42] "National Agency for Food and Drugs Administration and Control," NAFDAC
[43] "Research Ethics Committees in Nigeria: A Survey of Operations, Functions, and Needs"
[44] "Pharmaceuticals - South Africa: Statista Market Forecast," Statista
[45] "How the Pharmaceutical Industry Is Set to Rise in South Africa," Merchant Capital
[46] "Quality and Bioequivalence Guideline," SAHPRA

Local ECs in South Africa operate under the guidance of the National Health Research Ethics Council (NHREC) and are institution-based, responsible for monitoring studies conducted within their respective organizations. The South African Medical Association Research Ethics Committee (SAMAREC) holds national oversight for private-sector trials.[47]

Past MARA Therapeutics Trials

This section will provide a brief overview of two clinical trials previously conducted by MARA. Each summary highlights the trial's scope, outcomes, and key lessons learned.

LIVIN Trial

The **LIVIN trial** (1994-2003) evaluated alvdesivir for the treatment of HIV across a global cohort of participants 18 to 39 years old. The study was conducted in multiple countries, including the US, UK, Brazil, Peru, South Africa, India, Indonesia, and the Philippines. As one of MARA's largest trials to date, LIVIN significantly elevated the company's reputation in HIV research and catalyzed its expansion into broader infectious disease studies.

A notable innovation during this trial was the use of urban sites with integrated rural outreach networks. Sites in India, Indonesia, and Brazil were selected based on their existing local outreach programs that enabled MARA to collect data from a more diverse patient population. This approach not only enhanced trial inclusivity but also fostered community trust in the treatment. As a result, alvdesivir (PodzAir) saw higher acceptance and prescription rates in rural areas post-approval.

One major challenge was navigating the regulatory landscape across multiple countries. Prior to LIVIN, the company had only conducted trials in the US and secured approval for their first HIV treatment, gilentolimod, with the FDA. Efforts to secure gilentolimod approval from the EMA were hindered by limited trial diversity and insufficient data for European populations, necessitating an additional Phase III trial for EU approval. These regulatory lessons were incorporated into the LIVIN trial design, improving MARA's global approval strategy.

SHAW Trial

The **SHAW trial** was the company's most recent study conducted in Africa, among other regions, to expand ramafloxacin's indication for skin and soft tissue infections. The trial included adult participants 18 to 64 years old and was conducted in both urban and rural areas of Kenya, including underserved sites.

This trial was considered a major success for MARA for two primary reasons:

1. Demonstrated ramafloxacin's efficacy beyond pneumonia treatment

[47] "Clinical Trials Ethics in South Africa," SACRA

2. Provided valuable experience operating in a developing pharmaceutical market

During the trial, MARA partnered with KKB, a local pharmaceutical company in Kenya, to support professional development initiatives and to streamline the regulatory pathway for ramafloxacin's new indication. This collaboration both strengthened MARA's relationships with healthcare professionals in Kenya and enhanced its operational capabilities in emerging markets.

A significant challenge of the SHAW trial was patient recruitment, as many selected sites lacked robust outreach and screening procedures, ultimately leading to delays in enrollment. From this, MARA revised its site selection criteria to prioritize locations with established patient access and outreach infrastructure, ensuring smoother recruitment for future trials.

Case Competition: Key Questions and Considerations

Your challenge, as a participant in the 2025 Gilead Pharma Case Competition, is to make a series of recommendations to help assist MARA initiate its Phase III RESI trial. Focus on what you consider to be the key priorities, but include at least the following:

- **Projected Timeline:** Outline key site activation and patient enrollment milestones (e.g., first & last site activated, first & last patient in, enrollment targets) and consider how progress will be monitored
- **Site Prioritization and Selection** — *Refer to Exhibit I:* Recommend and justify prioritized and selected sites, considering factors that enable strong engagement throughout the trial
- **Risk Mitigation**: Identify key risks related to enrollment and site engagement, and propose strategies to minimize disruptions and maintain trial continuity
- **Treatable Patient Population** — *Refer to Appendix C & G***:** Calculate and describe the treatable MDR-TB patient population for ramafloxacin
- **Assumptions and Rationale:** Clearly state any assumptions & provide reasoning behind your strategic recommendations

You are welcome to conduct research in the public domain, though we recommend basing your ideas and recommendations primarily on what you read within this document.

If selected as a finalist, you will have 10 minutes to present to Steven A. Skiff and the MARA leadership team (case competition judges). They will then have 10 minutes to ask questions of your team and probe further into your recommendations and thought processes. Prepare your final PowerPoint deliverable with that in mind, as significant changes to the recommendations themselves will not be allowed once finalists are notified. All team members are expected to present during the presentation, and questions from judges may be asked directly to an individual or to the team, at large.

There is no single “right” answer. The judges are most interested in understanding your original ideas and the logic/rationale behind your overall strategy. Do not spend time researching the science behind the drug products themselves, as creative license was taken to provide approximations of real drugs for the context of this case competition. Therefore, that should not form the primary basis in your final deliverable.

Be creative, while also remembering to stay grounded in your recommendations.

Lastly, have fun and good luck!

-Gilead Case Competition Team

Appendix

A: Clinical Trial Stages[48]

B: Tuberculosis Treatment Regimens

Drug Regimens for Drug Susceptible TB[49]		
Regimen	**Intensive phase**	**Continuation phase**
Standard 6-month treatment (RIPE)	Rifampicin, Isoniazid, Ethambutol, Pyrazinamide (x8wks)	Rifampin, Isoniazid (x18wks)
Rifapentine-Based 4-month treatment	Rifapentine, Isoniazid, Moxifloxacin, Pyrazinamide (x8wks)	Rifapentine, Isoniazid, Moxifloxacin (x9wks)

Drug Regimens for Multidrug-Resistant TB[50]	
Criteria	**Regimen**
MDR-TB with fluoroquinolone susceptibility	BPaLM regimen: bedaquiline, pretonamid, linezolid, and moxifloxacin (x6months)
MDR-TB with preserved fluoroquinolone activity	Bedaquiline, levofloxacin/moxifloxacin, ethionamide, ethambutol, isoniazid high-dose, pyrazinamide, and clofazimine (x9months)
Individualized treatment	Customized regimens (usually x18months)

[48] "The Crucial End of Phase 2 FDA Meeting: A Drug Development Milestone," Bracken
[49] "TB Disease Treatment: 6- or 9-Month Ripe TB Treatment Regimen," Centers for Disease Control and Prevention
[50] "Treatment for Drug-Resistant Tuberculosis Disease," Centers for Disease Control and Prevention

C: Tuberculosis & Multidrug-resistant Tuberculosis Epidemiology

Country[51]	TB Instances per 100k	Total TB-related Deaths	MDR-TB Rate	MDR-TB Treatment Coverage (%)
Egypt	9	529	0.0099	88
Ethiopia	146	28,979	0.0136	72
Kenya	223	23,149	0.01	77
Morocco	92	1,925	0.0164	94
Nigeria	219	71,112	0.0188	74
South Africa	427	55,545	0.0495	79

*All data as of YE 2023

D: Country Population Statistics[52]

Country	Total Pop. (millions)	Pop. Density (per mi sq)	Urban Pop. (%)	Poverty Rate (%)	HAQ Index[53]
Egypt	114.5	280	43	29.7	73
Ethiopia	135.47	351	22.5	23.5	20
Kenya	57.53	262	31.9	38.6	33
Morocco	38.43	223	67.3	4.8	46
Nigeria	237.53	675	55.0	40.1	42
South Africa	64.75	138	66.6	55.5	24

*Data reflects latest available numbers as of July 2025

[51] "TB Profile," World Health Organization
[52] "African Countries by Population (2025) - Worldometer," Worldometer
[53] "Healthcare Access and Quality Index Based on Mortality from Causes Amenable to Personal Health Care in 195 Countries and Territories, 1990–2015: A Novel Analysis from the Global Burden of Disease Study 2015," Lancet

E: WHO Heath Authority Maturity Ratings

Country & Main Regulatory Authority	**WHO Maturity Level (I-IV)[54]** ***As of WHO ratings 2024**
Egypt – Egyptian Drug Authority	III
Ethiopia – Ethiopian FDA/Food, Medicine & Healthcare Administration and Control Authority	II
Kenya – Pharmacy & Poisons Board	II
Morocco – Pharmacy Division, Ministry of Health & Social Protection	II (Close to level III)
Nigeria – National Agency for Food & Drugs Administration and Control	III
South Africa – South African Health Products Regulatory Authority	III

WHO Maturity Level[55]	**Significance**
I	Indicates the existence of a regulatory system with some clear frameworks, such as national vigilance, corporate requirements, reporting procedures, etc.
II	Indicates an evolving regulatory system that partially performs essential functions, such as safety requirements and vigilance activities.
III	Indicates a stable, well-functioning integrated regulatory system. Clear requirements for conducting and reporting vigilance activity, standardized procedures for vigilance, and smooth communication between regulators and entities within the sector.
IV	The regulatory system in place is advanced and continuously updating/improving to adapt to new challenges. Implemented and enforced procedures for vigilance, and active monitoring systems are in place.

[54] "List of NRAS Operating At ML3 and ML4," World Health Organization
[55] "The Who Global Benchmarking Tool (GBT)," PAHO/WHO | Pan American Health Organization

F: Site Matrix Criteria Breakdown

	Infrastructure	PI Expertise	Patient Accessibility
5	State-of-the-art equipment (including diagnostics) and facilities	5+ years trial experience in MDR-TB	Central location, referral network, public transit accessible
4	New equipment (including diagnostics) and facilities	5+ years trial experience in ID	2/3 of the above criteria
3	Functional equipment and facilities with limited capacity	1-2 years trial experience in ID	1/3 of the above criteria
2	Older equipment and facilities have capacity for basic healthcare needs	0 trial involvement but adequately trained	1/3 with increased barriers
1	Old and/or malfunctioning equipment with limited facility capacity	Limited to no understanding of conducting trials	0/3 with barriers

Note: These ratings were based on research done in the public domain as well as based on information from various individuals with experience working in these fields. They are meant to provide a standard review of each CT site relative to the others.

G: Treatable Patient Population Calculation & Estimated Market Share[56]

To calculate the estimated treatable patient population, the following formula may be used to obtain an estimate:

$$\text{TB instances total} * \text{MDRTB rate} * \text{Treatment coverage rate} * \text{Additional special considerations or criteria} = \text{Treatable Patient Population}$$

The current standard of care for MDR-TB (BPaLM regimen) is expected to capture 78% of market share in 2026. The BPaLM regimen has captured most of the market share because of recent WHO guideline updates promoting it as first line. The remaining market share includes all-oral bedaquiline-based treatment regimens (15%) and individualized treatment regimens (7%).[57]

[56] "The State of Clinical Trial Activation at Sites," Advarra
[57] "Global Adoption of 6-Month Drug-Resistant TB Regimens: Projected Uptake by 2026"

Company Profile

Company Name	MARA Therapeutics
Established Date	1987
Sector	Biotechnology
Headquarters	Boston, Massachusetts
No. of Employees	6,000
Therapeutic Areas	Virology, Infectious Disease

Financials at a Glance:

MARA
NASDAQ

$23.11 Bn
2024 Revenue

$3. 67 Bn
2024 Net Profit

Workplace Awards

Company Milestones

1987
MARA Therapeutics founded

1995
Gilentolimod FDA-approval

2002
Ramafloxacin approved for CAP

2004
MARA Therapeutics goes public

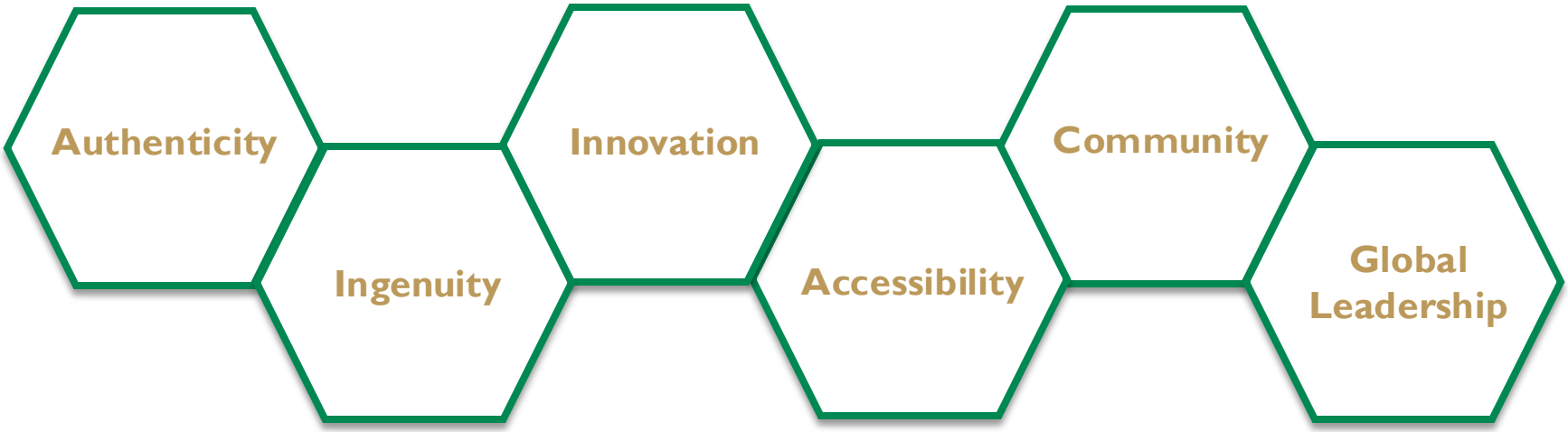
2018
MARA shifts R&D focus to MDR-TB

MARA Therapeutics

Company Ethos & Mission Statement

MARA Therapeutics was founded with a mission to develop effective and accessible treatments for diseases that disproportionately impact the world's most vulnerable populations. We believe that improving global health outcomes requires bold innovation and a commitment to equity, ensuring that life-changing solutions reach everyone who needs them.

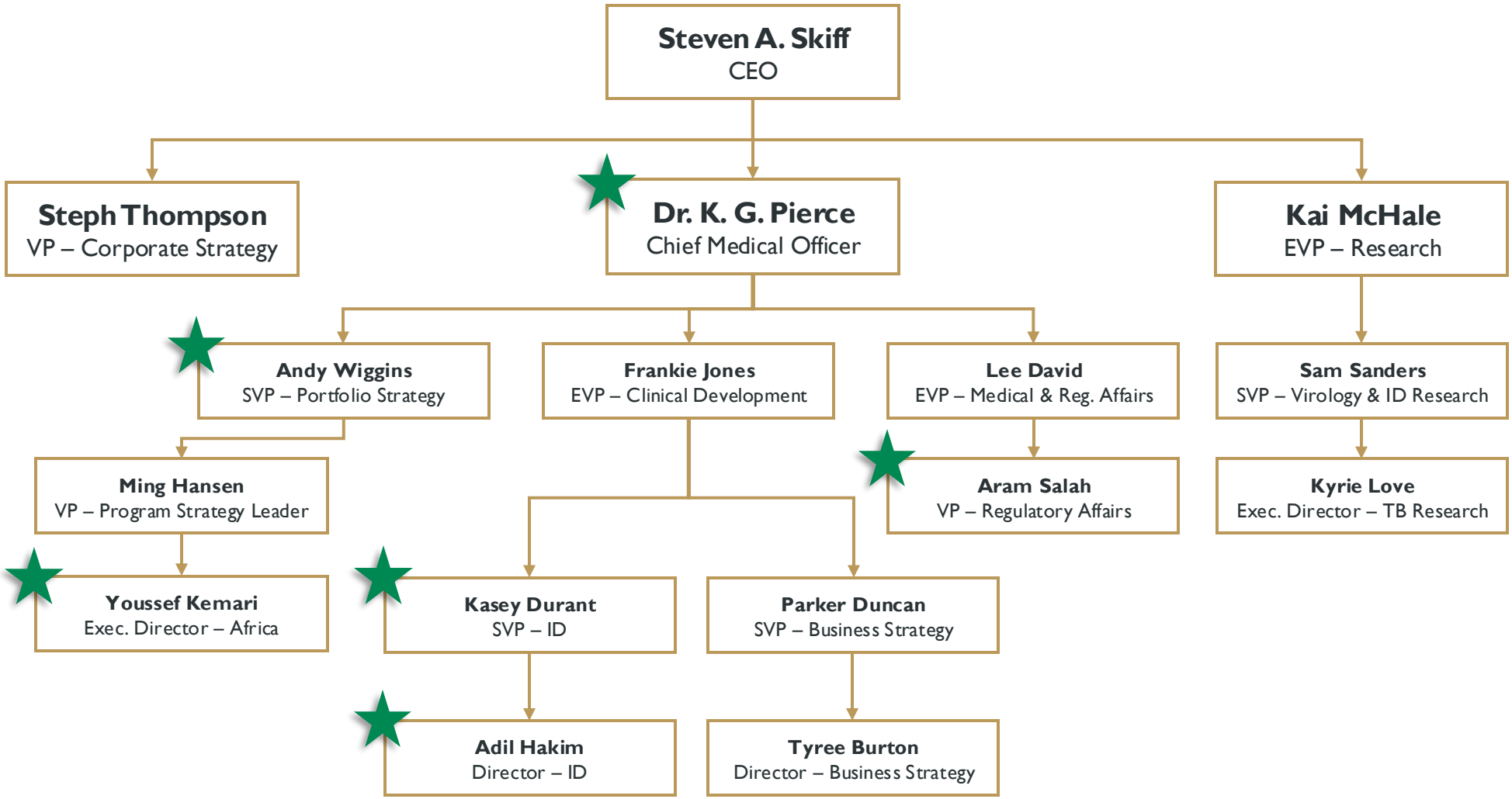
Core Values:



Mission Statement:

For 38 years, MARA Therapeutics has been a global leader in developing treatments for resistant diseases. Guided by our core values, we remain committed to delivering high-quality therapies that advance global public health and improve outcomes for all.

Organization Chart



Acronyms: ED (Executive Director), (E/S/J)VP (Exec./Senior Vice President), ID (Infectious Disease)
Green stars indicate members of the trial leadership team, chosen based on their positions in the company and relevant expertise to the project.

Pipeline

Virology

Target Indication (Study Name)	Compound	Phase I	Phase II	Phase III	Phase IV
HIV Treatment (KEV)	Gilentolimod				
HIV Treatment (LIVIN)	Alvdesivir				
HIV Post-Exposure Prophylaxis (POST)	Aurocapavir				Filed

Infectious Disease

Target Indication (Study Name)	Compound	Phase I	Phase II	Phase III	Phase IV
Community-Acquired Pneumonia (TOON)	Ramafloxacin				
Skin and Soft Tissue Infections (SHAW)	Ramafloxacin				
Multidrug-Resistant Tuberculosis (RESI)	**Ramafloxacin**			Planned	
Multi-Drug-Resistant Tuberculosis (KALM)	Armafloxacin				
Multidrug-Resistant Tuberculosis (MACAW)	Maraquiline				
Complicated Urinary Tract Infections (SAS)	Wembamycin				
Endocarditis (BUCK)	Thanasimycin				
Endocarditis (MEMPH)	Edeyfloxacin				

Ramafloxacin Product Overview

Drug Name	**Ramafloxacin**
Classification	**Fluoroquinolone antibacterial**
MoA*	**Inhibition of DNA synthesis**
Dosing	**One tablet by mouth once daily**

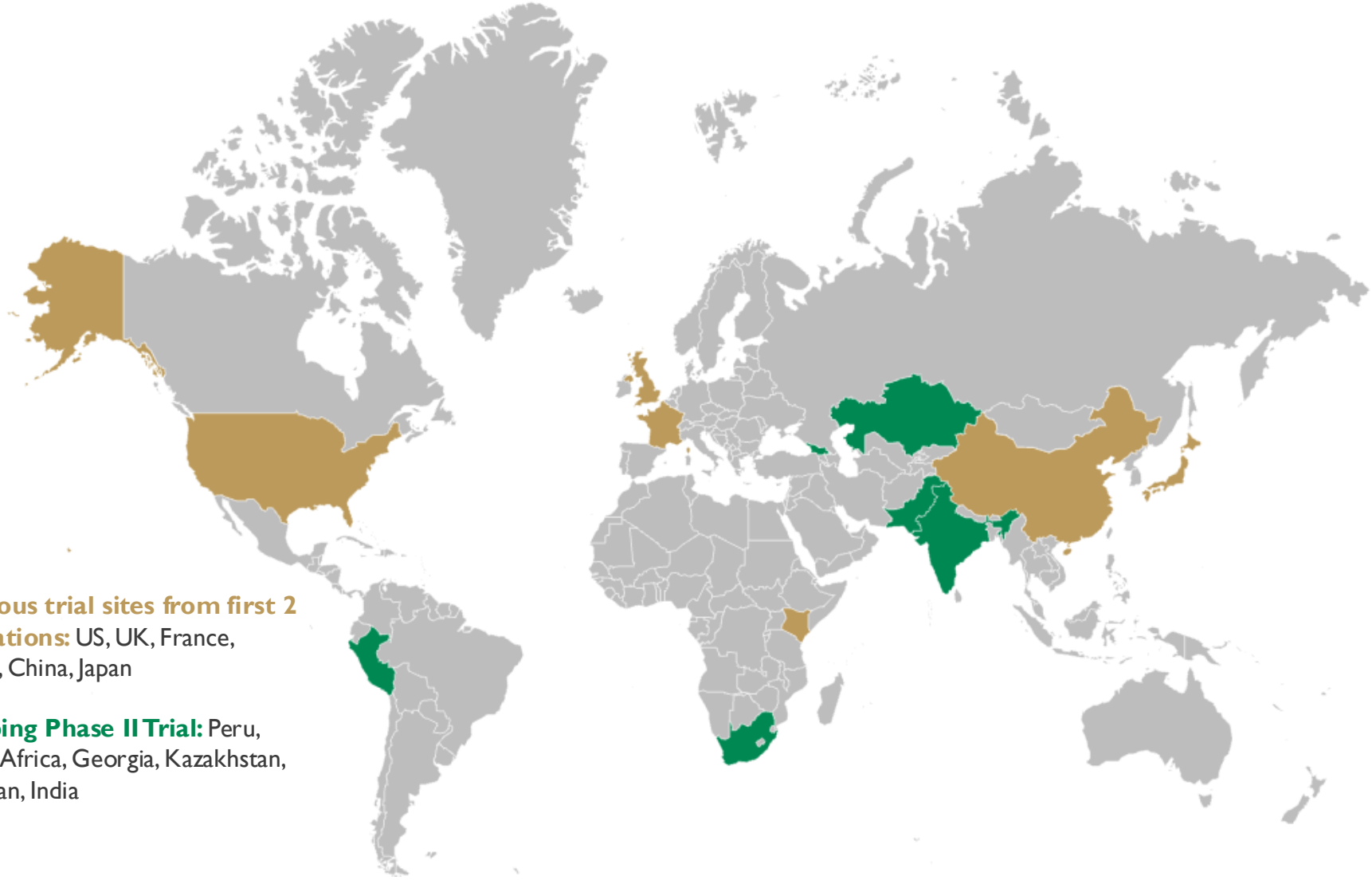
Indication	Status	Treatment Regimen
Community-Acquired Pneumonia	Approved in 2002	Used as monotherapy or in combination with MRSA and/or Gram-Positive agents
Skin and Soft Tissue Infections	Approved in 2016	Used as monotherapy or in combination with MRSA and/or Gram-Positive agents
Multidrug-Resistant Tuberculosis	**Ongoing Phase II; Planned Phase III**	**Used in combination with BPaL antibacterial agents^**

*Mechanism of Action

^Other medications (bedaquiline, pretonamid, linezolid) in the trial are provided in collaboration with other pharmaceutical companies

MARA Therapeutics

Ramafloxacin has previously undergone clinical trials conducted across multiple regions.



Previous trial sites from first 2 indications: US, UK, France, Kenya, China, Japan

Ongoing Phase II Trial: Peru, South Africa, Georgia, Kazakhstan, Pakistan, India

MARA Therapeutics

MARA Therapeutics ranked *10th* on the *2024 Access to Medicines Index.*

We are committed to improve health outcomes in LMICs. The ranking reflects our dedication in medication access. We aim to strengthen R&D efforts in countries with an ***unmet medical need****.*

access to medicine FOUNDATION

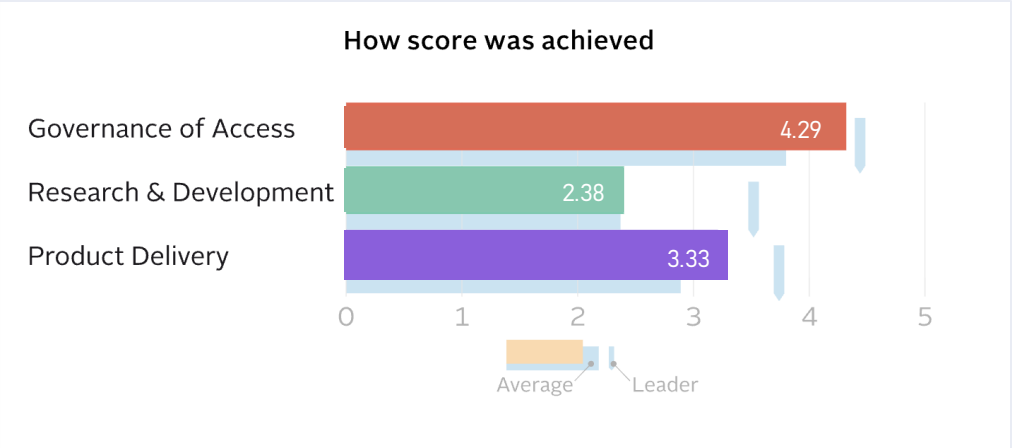
MARA Therapeutics

Stock exchange: NASDAQ · Ticker: MARA · HQ: Boston, Massachusetts ·

ACCESS TO MEDICINE INDEX

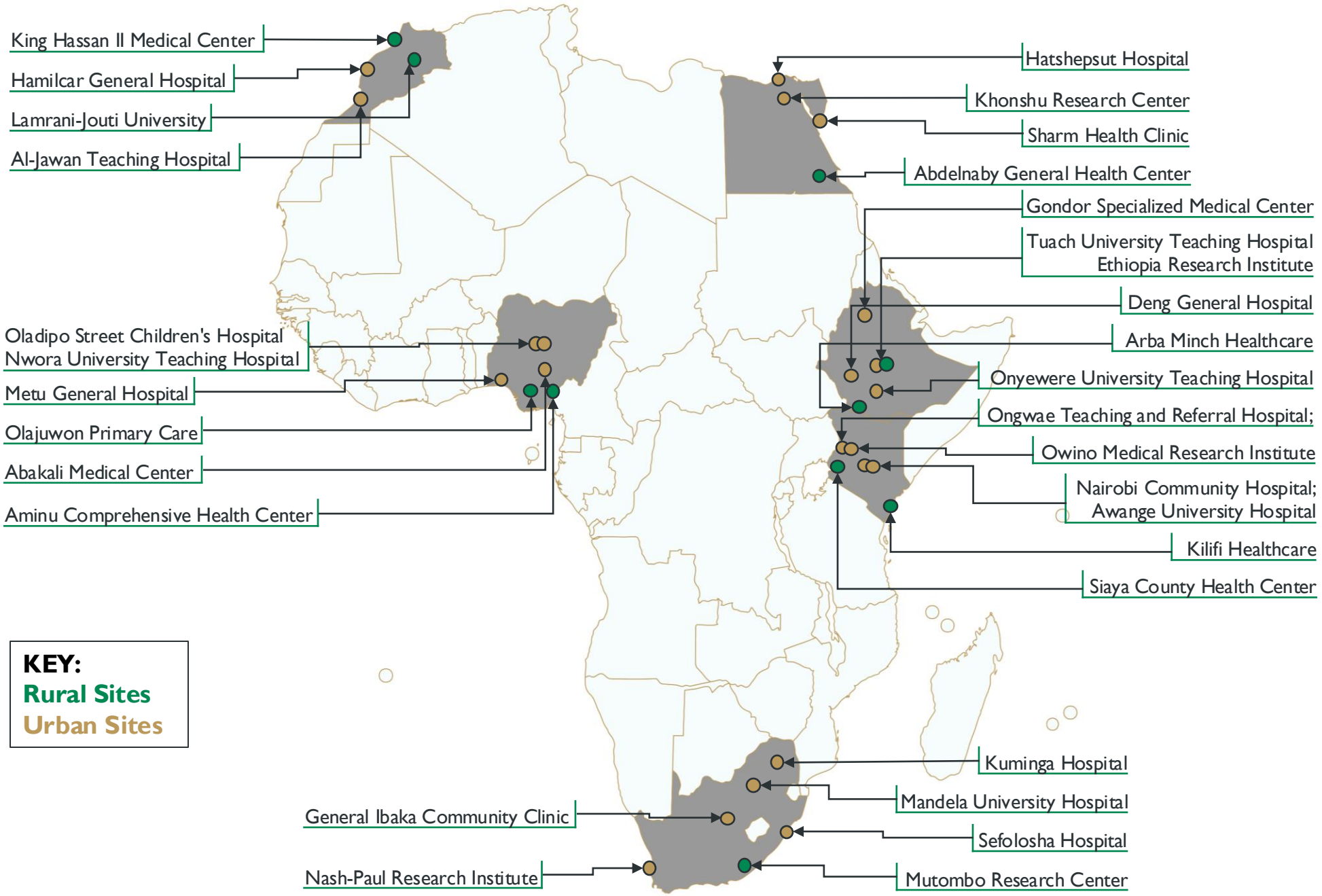
Performance in the 2024 Index

10th place. MARA Therapeutics ranks in the top ten. It has improved its performance in Governance of Access. The company performs above average in Research & Development and Product Delivery, where it shows Best Practice in registering innovative products broadly in low- and middle-income countries (LMICs).



MARA Therapeutics

Africa Site Map



MARA Therapeutics

Potential Clinical Trial Sites in Africa

Site Name	Country	Location	Site Type	Regulatory Compliance
Sharm Health Clinic	Egypt	Sharm (urban)	Community health clinic	Meets standard local guidelines
Khonshu Research Center	Egypt	Cairo (urban)	Research institute	Frequent inspections
Alexandria Hospital	Egypt	Alexandria (urban)	Hospital	Passed recent inspection
Abdelnaby General Health Center	Egypt	Aswan (rural)	Medical center	Requires GCP and regulatory guidance
Tuach University Teaching Hospital	Ethiopia	Addis Ababa (urban)	University hospital	Frequent inspections
Deng General Hospital	Ethiopia	Jimma (suburban)	Medical center	Meets standard local guidelines
Gondor Specialized Medical Center	Ethiopia	Gondar (urban)	Medical center	Passed recent inspection
Onyewere University Teaching Hospital	Ethiopia	Awasa (rural)	University hospital	Meets standard local guidelines
Arba Minch Healthcare	Ethiopia	Arba Minch (rural)	Hospital	Meets standard local guidelines
Ethiopia Research Institute	Ethiopia	Addis Ababa (urban)	Research institute	No previous inspection
Nairobi Community Hospital	Kenya	Nairobi (urban)	Hospital	Frequent inspections
Awange University Hospital	Kenya	Nairobi (urban)	University hospital	Meets standard local guidelines
Ongwae Teaching and Referral Hospital	Kenya	Eldoret (urban)	University hospital	Meets standard local guidelines
Owino Medical Reseach Institute	Kenya	Eldoret (urban)	Government institute	Frequent inspections
Kilifi Healthcare	Kenya	Kilifi (rural)	Medical center	Requires GCP and regulatory guidance
Siaya County Health Center	Kenya	Siaya (rural)	Medical center	No previous inspection
Al-Jawan Teaching Hospital	Morocco	Agadir (urban)	Hospital	Frequent inspections
King Hassan II Medical Center	Morocco	Rabat (rural)	Medical center	Requires GCP and regulatory guidance
Lamrani-Jouti University	Morocco	Fes (rural)	University medical center	Meets standard local guidelines
Hamilcar General Hospital	Morocco	Marrakech (urban)	Hospital	Requires GCP and regulatory guidance
Nwora University Teaching Hospital	Nigeria	Abuja (urban)	University	Frequent inspections
Aminu Comprehensive Health Center	Nigeria	Ikom (rural)	Community health clinic	No previous inspection
Olajuwon Primary Care	Nigeria	Abiriba (rural)	Medical center	Requires GCP and regulatory guidance
Oladipo Street Children's Hospital	Nigeria	Abuja (rural)	Hospital	Frequent inspections
Abakali Medical Center	Nigeria	Abakaliki (rural)	Research institute	Passed recent inspection
Metu General Hospital	Nigeria	Lagos (urban)	Hospital	Meets standard local guidelines
Mandela University Hospital	South Africa	Johannesburg (urban)	University medical center	Frequent inspections
Mutombo Research Center	South Africa	Ndevana-East London (rural)	Research institute	Meets standard local guidelines
Sefolosha Hospital	South Africa	Durban (rural)	Hospital	Passed recent inspection
Nash-Paul Research Institute	South Africa	Cape Town (urban)	Research institute	Passed recent inspection
General Ibaka Community Clinic	South Africa	Bloemfontein (rural)	Community health center	Meets standard local guidelines
Kuminga Hospital	South Africa	Pretoria (urban)	Hospital	Passed recent inspection

Refer to Appendix F for Site Matrix Criteria

Potential Clinical Trial Sites in Africa

Site Name	Ethics Committee	Infrastructure	PI Experience	Patient Accessibility
Sharm Health Clinic	Local	5	2	5
Khonshu Research Center	Institutional	5	1	4
Alexandria Hospital	Local	3	4	4
Abdelnaby General Health Center	Local	1	3	3
Tuach University Teaching Hospital	Institutional	5	5	5
Deng General Hospital	Institutional	4	3	4
Gondor Specialized Medical Center	Institutional	2	3	4
Onyewere University Teaching Hospital	Local	3	3	3
Arba Minch Healthcare	Local	2	2	2
Ethiopia Research Institute	Local	5	1	4
Nairobi Community Hospital	Local	5	1	5
Awange University Hospital	Institutional	5	2	4
Ongwae Teaching and Referral Hospital	Institutional	4	3	4
Owino Medical Reseach Institute	Institutional	5	5	3
Kilifi Healthcare	Local & Institutional	2	2	2
Siaya County Health Center	Local	1	1	4
Al-Jawan Teaching Hospital	Local	4	4	5
King Hassan II Medical Center	Institutional	5	3	5
Lamrani-Jouti University	Local	3	3	4
Hamilcar General Hospital	Local	5	2	4
Nwora University Teaching Hospital	Institutional	5	2	5
Aminu Comprehensive Health Center	Institutional	2	2	4
Olajuwon Primary Care	Local	4	3	2
Oladipo Street Children's Hospital	Institutional	5	4	4
Abakali Medical Center	Institutional	5	5	4
Metu General Hospital	Local	3	3	3
Mandela University Hospital	Institutional & National	5	3	5
Mutombo Research Center	National	3	3	4
Sefolosha Hospital	Institutional & National	4	5	4
Nash-Paul Research Institute	Institutional & National	5	2	5
General Ibaka Community Clinic	National	2	2	4
Kuminga Hospital	Institutional & National	2	3	3

Potential Clinical Trial Sites in Africa

Site Name	Estimated Patient Pool	Estimated Time to Activation	Additional Site Considerations
Sharm Health Clinic	0-15	90-150 days	Will require additional training on CT conduct
Khonshu Research Center	0-10	60-150 days	High data quality but limited to no CT experience
Alexandria Hospital	0-10	30-90 datys	Previous MARA experience in virology
Abdelnaby General Health Center	0-5	60-120 days	Strong rural community network
Tuach University Teaching Hospital	20-80	90-120 days	Competing ongoing MDR-TB trial
Deng General Hospital	20-50	90-180 days	Specialized diagnostic equipment required
Gondor Specialized Medical Center	0-30	30-90 days	Primarily cardiology patient population
Onyewere University Teaching Hospital	10-40	30-90 days	Study similar to prior virology CT
Arba Minch Healthcare	0-30	60-150 days	Extra facility requirements needed
Ethiopia Research Institute	40-80	120-180 days	Need to up-skill staff given limited to no CT experience
Nairobi Community Hospital	40-80	90-180 days	Strong community network involvement
Awange University Hospital	30-70	30-120 days	Overlapping clinical trial in TB
Ongwae Teaching and Referral Hospital	30-70	60-120 days	Study similar to prior virology CT
Owino Medical Reseach Institute	10-40	60-150 days	Extra facility requirements needed
Kilifi Healthcare	10-40	90-180 days	Previous MARA experience in ID
Siaya County Health Center	30-80	180+ days	Previous MARA experience in ID
Al-Jawan Teaching Hospital	0-20	30-90 days	Previous TB trial with some data quality concerns
King Hassan II Medical Center	0-10	60-120 days	Strong community network involvement
Lamrani-Jouti University	0-10	60-180 days	Previous CT experience in diabetes
Hamilcar General Hospital	0-20	90-180 days	Previous MARA experience in virology
Nwora University Teaching Hospital	50-100	90-180 days	Slow EC turnaround; MD staffing concerns
Aminu Comprehensive Health Center	40-80	120-180 days	Strong community network involvement
Olajuwon Primary Care	0-50	60-150 days	One previous CT had enrollment difficulties
Oladipo Street Children's Hospital	0-50	30-90 days	Patient population only consists of pediatrics
Abakali Medical Center	0-80	30-120 days	Overlapping clinical trial in TB
Metu General Hospital	25-50	60-150 days	Some experience with virology trials
Mandela University Hospital	50-100	45-105 days	Staffing concerns may limit trial activation
Mutombo Research Center	40-80	60-120 days	Previous CT experience in ID
Sefolosha Hospital	20-60	30-90 days	Overlapping clinical trial in TB
Nash-Paul Research Institute	50-100	60-120 days	No competing trials but CT experience is very limited
General Ibaka Community Clinic	40-80	91-150 days	Minimal CT experience, extra facility requirements
Kuminga Hospital	40-60	30-60 days	Previous CT experience in DR-TB trials

Country-Specific Considerations

Below is a comparison chart populated by MARA Dev LT, based on publicly available information and general guidance from local connections.

Country	Ease of Import & Distribution to Sites	Local Patient Data Required?
Egypt	**Moderate,** require detailed documentation and regulatory clearance	**Not strictly required,** local bridging studies may be requested
Ethiopia	**Challenging,** can be slow due to customs and regulatory bottlenecks	**Not explicitly required,** strict rules on foreign-sponsored trials; local CRO involvement is encouraged
Kenya	**Moderate to easy,** streamlined procedures and growing logistics network	**Not mandatory,** local trials are preferred for registration
Morocco	**Moderate,** regulated but manageable	**Generally not required,** local studies may be requested depending on TA
Nigeria	**Challenging,** complex due to regulatory layers and fragmented networks	**May be required,** often requires local data or bridging studies
South Africa	**Easy,** well-established systems and strong logistics infrastructure	**Often required,** strong clinical trial infrastructure

LT Whiteboard Exercise: RESI Trial

Nigerian NHSRI Initiative has provided funding for several hospitals in Lagos to upgrade infrastructure and hire more research staff
– Adil Hakim

Ethiopian govt. tax & financial measures to promote domestic pharma would reduce some costs for both the trial and manufacturing plans. Worth keeping in mind.

Egypt's reputation as a reliable producer, and their exports to the Middle East would boost our profile in the region if ramafloxacin was approved and made there.
– Steph Thompson

Our partner CROs for the trial have more experience in Egypt, South Africa and Ethiopia. Worth considering for potential setbacks due to unfamiliarity.
– Steven A. Skiff

Concentration of Kenyan pharma in Nairobi would make rural access tougher to balance with facility quality and trial conduction.
– Kasey Durant

South Africa sites were extremely successful for SHAW trial, equipment and staff concerns were often minimal or nonexistent compared to Kenyan sites.
– Kai McHale

Leveraging our experience and familiarity with Kenya would help our efforts to grow our LMIC presence in East Africa. Also, would reveal any roadblocks.
– Steven A. Skiff

Transportation difficulties in Nigeria have slowed down trials in the past. If we want to work there, we should pick sites in urban areas to avoid some of those issues.
– Adil Hakim

Getting approval from the Moroccan reg. system would allow for expedited manufacturing and international distribution post-study
– Aram Salah

South Africa's high MDR-TB numbers present a guaranteed market for us post trial, which the commercial team is interested in. Already spoke to Steph abt. this too.
– Tyree Burton

Nigeria's overlapping health concerns besides TB might limit the focus and resources available for our trial. Should look more into this before deciding.
– Dr. Pierce

South Africa's patient availability in both urban and rural areas suggests a much shorter recruitment timeline. Nigeria also has similar concentration of cases.
– Kasey Durant

Kilinto Industrial Park would be an attractive place to manufacture in the near future, should look more into building footprint in Ethiopia through RESI trial.
– Andy Wiggins

Analysis of HIV Tx adoption in Ethiopia and Nigeria suggest favorable conditions for early implementation. Strong potential for uptake and engagement if operational plans are aligned with regional needs and infrastructure.
– Tyree Burton

Moroccan health dept. announcement from July sounds promising for their healthcare industry. Worth considering for future distribution efforts for gilentolimod.
– Steph Thompson

Egyptian govt. investment in pharma production ingredient purchases, and other financial support for domestic pharma a potential roadblock to future operations there
– Andy Wiggins

South Africa & Nigeria represent higher HIV case volumes, among others. Sustained uptake and engagement may be more guaranteed compared to other regions.
– Steph Thompson

Familiarity with urban sites in Kenya from SHAW trial – we know the investigators and HCPs at some of the sites and they in turn know our company. Could help with reg. timeline post-study
– Adil Hakim

MARA Therapeutics

Lessons Learned from Past Trials

Trial Logistics…

- ✓ Transportation infrastructure and logistics should be near the top of considerations when selecting rural trial sites: if we can't get there easily, patients probably won't be able to either.
- ✓ Beyond the actual clinical equipment and infrastructure, adequate cold storage should be a primary consideration when exploring sites: does the site have cold storage on-site? If not, is there an available cold storage location nearby?

…Site Selection & Patient Enrollment…

- ✓ Although urban sites in LMICs usually have better equipment and experience than rural ones, they often get saturated with multiple studies at a time, which creates timeline delays and can result in mistakes.
- ✓ In LMICs, using community-based organizations and networks can speed up recruitment, and even lead to higher sales post-trial. Religious organizations retain high levels of trust in LMICs and can help build credibility of the company, the trial, and the drug.

… and Regulatory Considerations

- ✓ Picking countries where we have existing relationships in the healthcare sector and regulatory system speeds up approval timelines significantly.
- ✓ Less developed regulatory systems usually correlate with inexperienced domestic investigators and ECs. This shouldn't be a disqualification for certain countries, but something to consider.

Competitive Landscape

These five projects in similar therapeutic areas and regions as the RESI trial have caught the company's attention, and the corporate strategy department is actively monitoring them.

Company	Project Type	Status	Countries	Size & Scope	Notes & Considerations
AI3 LTD. TRANSFORMING HEALTHCARE THROUGH AI SOLUTIONS	Phase III clinical study (TB vaccine)	Ongoing	Morocco, Kenya, Zambia, DRC, Cameroon	2500+ patients	Possible site overlap in Morocco & Kenya in urban centers 6-month results showing 65% efficacy rates in adults, and 72% in adolescents
DNLD PARTNERS SINCE 1993	Rapid diagnosis system for MDR-TB	Ongoing	South Africa, Nigeria, DRC, Ethiopia, Ghana	1000-1200 patients	Patient pool competition a possibility, however, would likely not be a major issue for site selection consideration, and could even be helpful in discovery.
GAINTE BIOTECH CRAFTING MEDICAL SOLUTIONS SINCE 1999	Phase II clinical study (COPD treatment)	Planned start in Q3 2026	South Africa, Ethiopia, Nigeria	400-500 patients	Not anticipated to be a barrier for RESI, but could become a possible thorn for site usage, equipment, etc.
NJXU SCIENCES MARKET-LEADING MEDICATIONS SINCE 2004	Phase III clinical study (HIV prevention)	Starting in Q1 2026	South Africa, Mozambique, Zambia, Kenya	1500 patients	Minimal overlap with RESI anticipated, however the company announced plans for multiple rural sites across the 4 countries.
SCKT BIOSOLUTIONS REVOLUTIONARY TREATMENTS SINCE 2011	Phase II clinical study (Pulmonary TB)	Planned start in Q4 2025	Egypt, Kenya, Nigeria, DRC	300+ patients	Patient overlap anticipated, could slow down recruitment. Possible regulatory backlog due to overlapping disease state.