

Evaluation of Clinical Trial Sites and Strategy | Phase III RESI Trial

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Executive Summary



The total **treatable MDR-TB population** in the 6 target African countries is **19,930 annually**

- **South Africa and Nigeria account for 83.5% of total disease burden**



South Africa, Nigeria, Morocco and Ethiopia are the most **viable countries for RESI phase - III trial** due to:

- High disease burden
- Robust supply chain and operational feasibility
- Clear pathway to commercialization



We recommend a **12-site portfolio activated in three strategic waves**

- Fast-track: for early launch of clinical trial
- Standard: to drive up patient volume
- Complex: as strategic sites for competitive advantage

This timeline ensures rapid start up with First Patient In achieved in Q4'26, followed by Last Patient In milestone by Q4'27



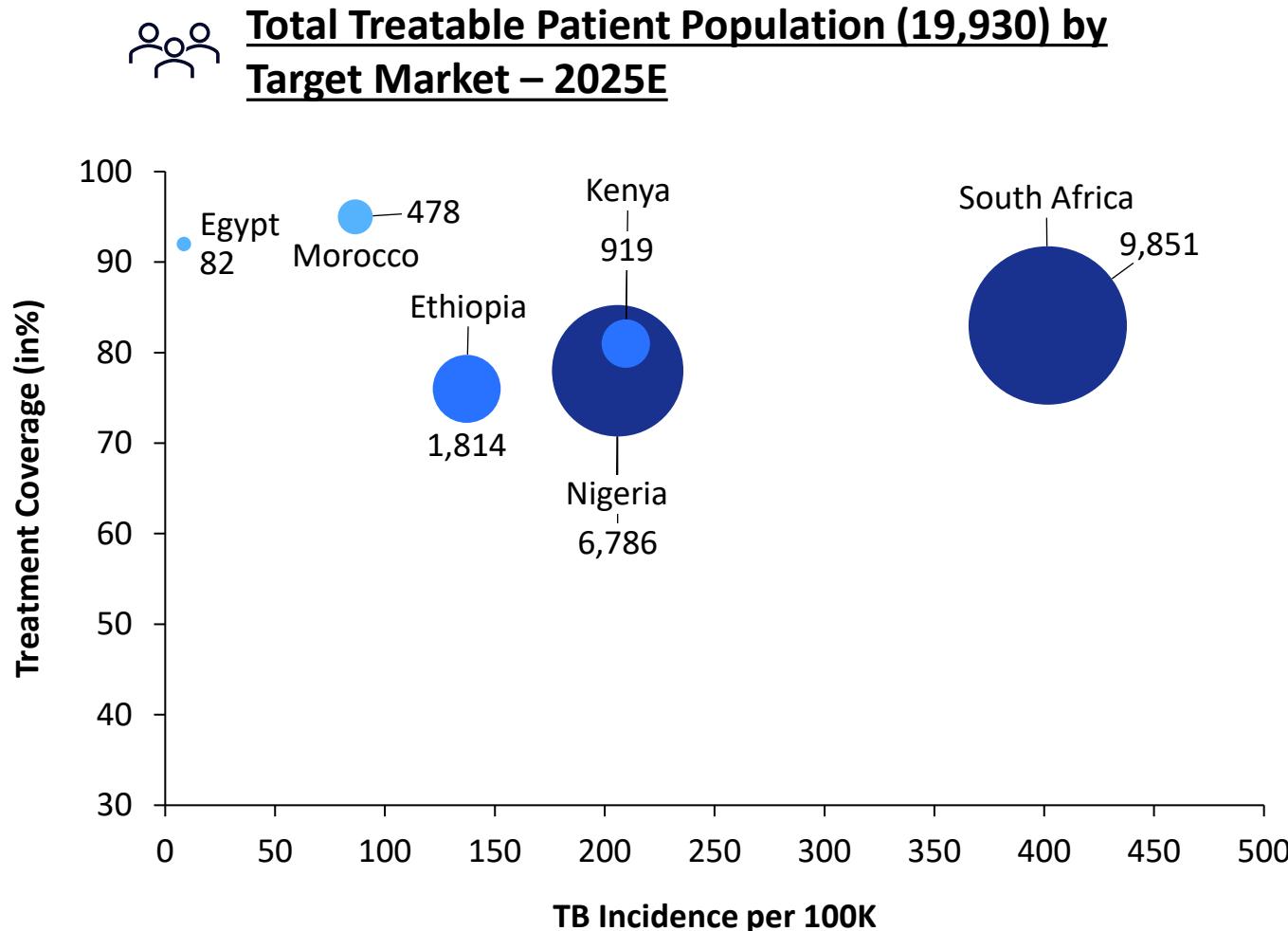
Key risks of **site competition** from overlapping sites and **PI inexperience** at few high-potential locations will be mitigated by **funding dedicated study coordinators**, implementing enhanced **monitoring plans with community engagement**



Focus Where The Need Is Greatest

Total Treatable Patient Population | By Target Markets

South Africa and Nigeria account for ~83% of MDR-TB cases among the target countries



Key Insights

- **High volume markets:** High TB incidence that are viable spots for RESI phase - III trial
- **High function markets:** Excellent healthcare infrastructure with advanced regulatory systems that offer a clear pathway to commercialization



South Africa



Nigeria



Morocco

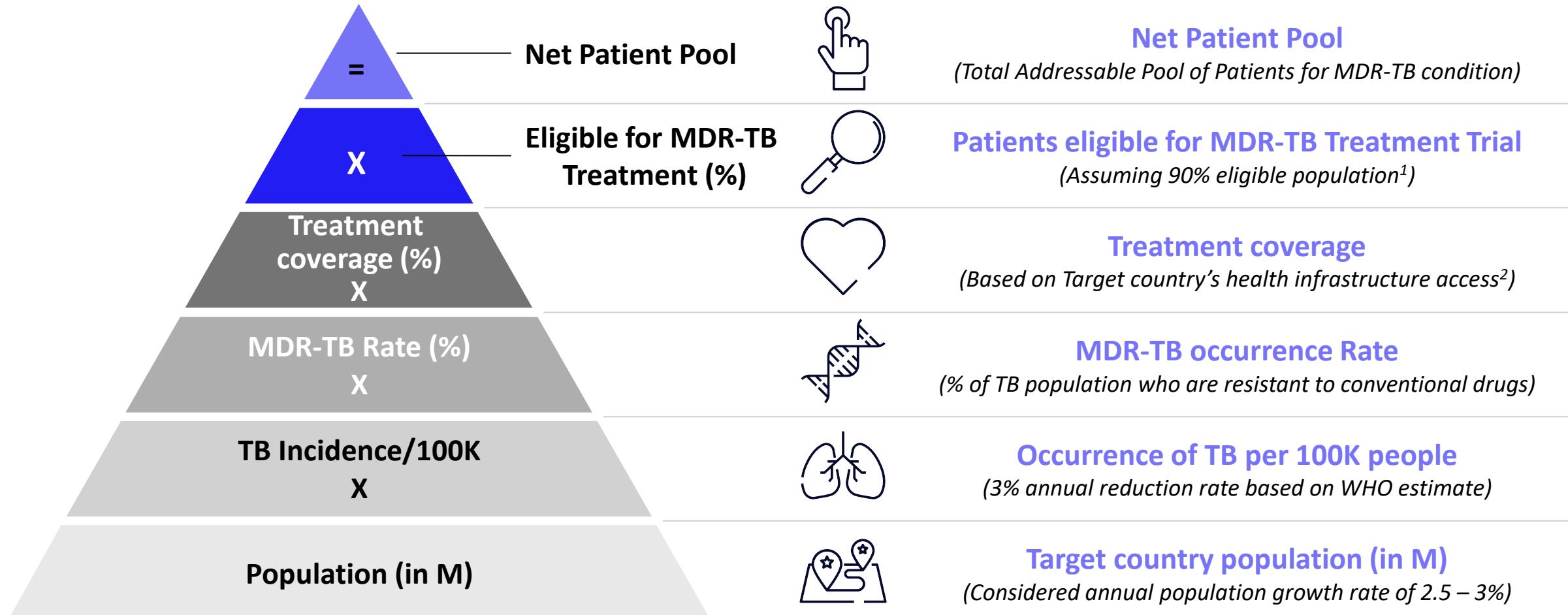


Egypt

1. In 6 target countries in Africa; Source: TB Profile, World Health Organization; Worldometer; Healthcare access and Quality Index – 2025; Assumption: Based on UN World Population prospects, expected annual population growth of 2.5% with 3% decline in TB case incidences and 4% improvement in patient accessibility to healthcare

Calculated treatable patient pool for 2025 based on health indicators and growth estimates

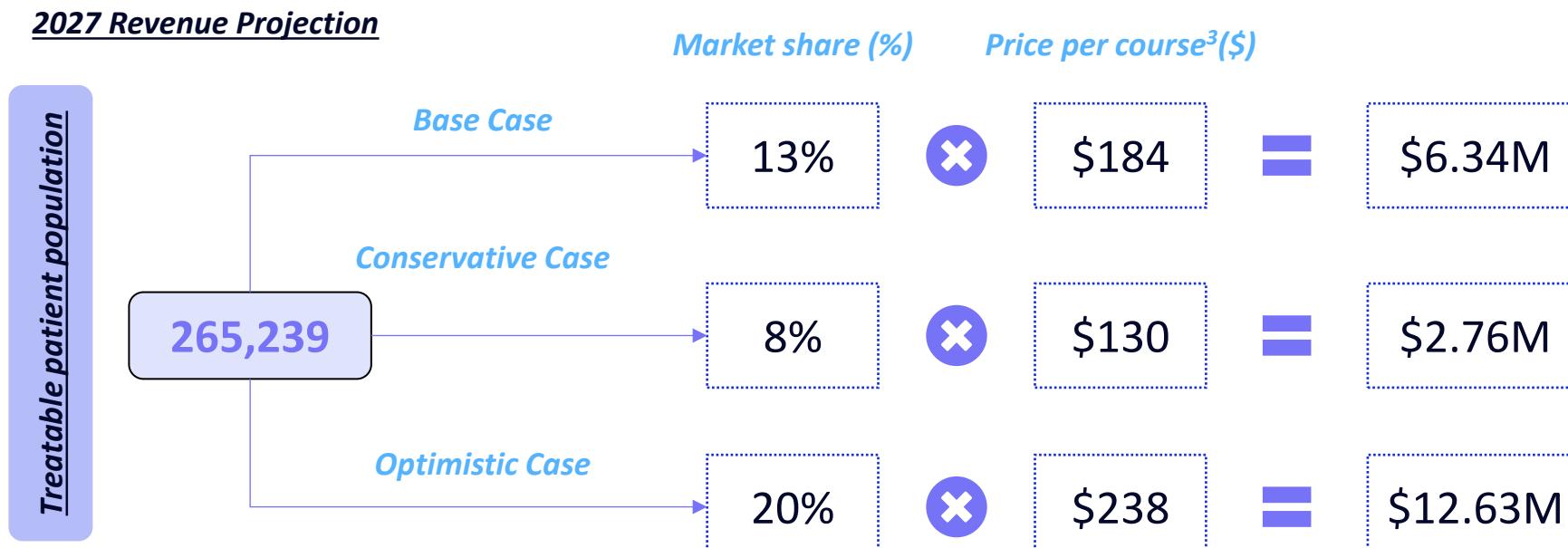
Projection for 2025 Treatable Patient Pool = Population x (TB Incidence/100,000) x MDR-TB Rate x Treatment Coverage x Eligible for MDR-TB Treatment



Source: 1. Accounting for co-morbidities and Ramafloxacin resistance; [American Journal of Respiratory and Critical Care Medicine](#); TB Profile, World Health Organization; Worldometer; 2. Expected to improve by 2% annually; Healthcare access and Quality Index – 2025; 3. Based on World Population Prospects for 2025 projection; Assumption: Based on [UN World Population prospects](#), expected annual population growth of 2.5% with 3% decline in TB case incidences and 4% improvement in patient accessibility to healthcare

Ramafloxacin is expected to bring in ~\$6 - \$13M annually for MDR-TB treatment with potential to upsell and diversify for other treatments

Metric	2023 Baseline	Annual growth rate	2027 Projection
Global MDR-TB Incidence	400,000 ¹	0.5% ²	408,060
Total Treatment Coverage	44% ¹	12% ³	65%
Total Treatable Patients	176,000	3.5%	265,239



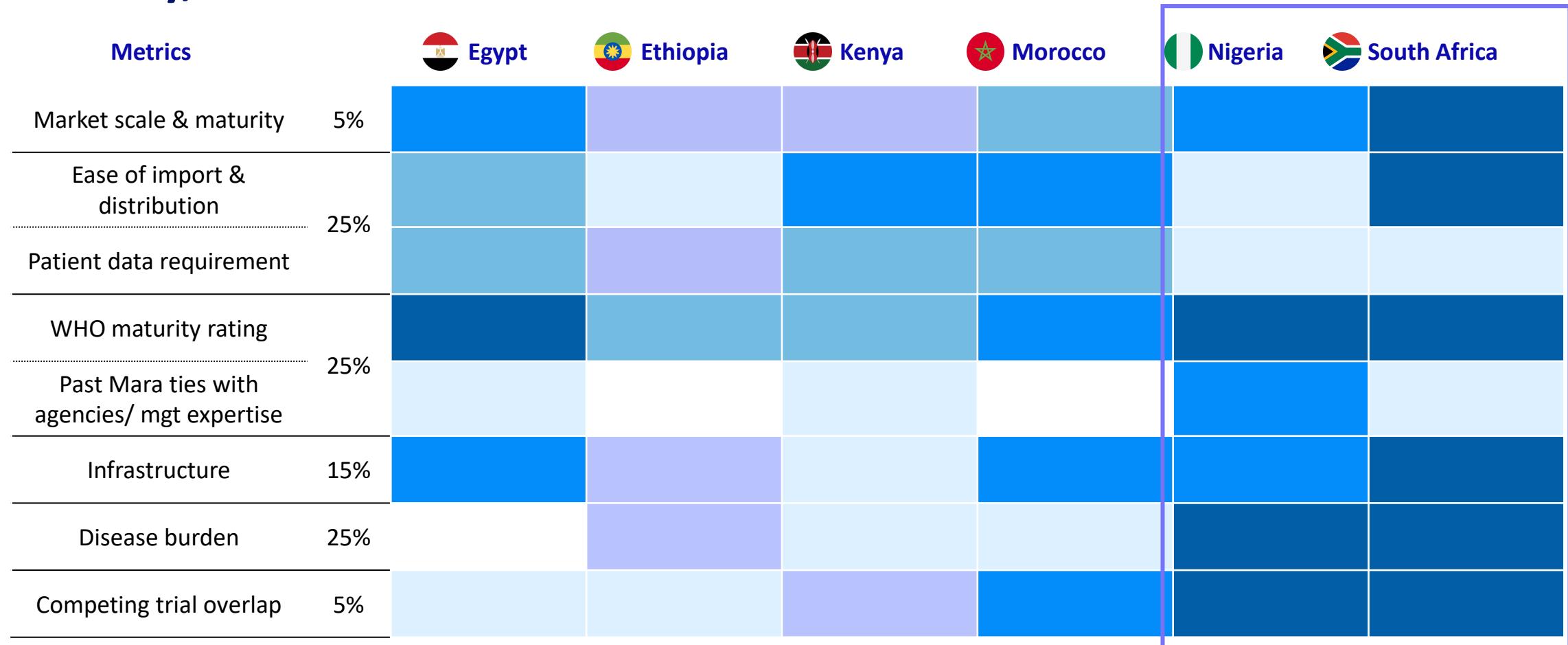
Source: 1. [WHO Global Tuberculosis Report](#); 2. Stable with slight population driven increase based on World Population Prospects estimate; 3. 12% YoY growth in total treatment coverage based on improvement in health infrastructure due to government funding and investments; Based on innovative drugs in the MDR-TB regimen like Bedaquiline (\$130/course) or Pretomanid (\$238/course) for typical 6 months course



Bringing Hope Where It's Needed Most

Site Prioritization and Selection | By Select Countries

Country Screening | South Africa and Nigeria emerged as clear winners in the scorecard based on operational feasibility, regulatory maturity, disease burden



Balancing high volume market for patient enrollment with high function markets for post commercialization distribution is critical for RESI trial's success.

Country Screening | Morocco and Ethiopia are the strategic fit for RESI trial based on cost efficiency and post commercialization pathway

Countries	Patient Pool ¹	Rationale
 Morocco	1,814	<ul style="list-style-type: none"> International trust and credibility: Advanced regulatory system recognized by FDA/EMA Ease of distribution: Expedited manufacturing and international distribution post study Operational stability: Manageable import and distribution; high domestic production of drugs (65-70%)
 Ethiopia	919	<ul style="list-style-type: none"> Cost efficiency: Government offers tax benefits that reduces trial and manufacturing costs Future manufacturing hub: Kilinto Industrial Park – viable for manufacturing Partner experience: CROs have significant experience that reduces potential setback
 Kenya	478	<ul style="list-style-type: none"> Enrollment risk: 18% of population do not meet WHO criteria for patient accessibility Geographic risk: High concentration of facilities in Nairobi Delayed drug approval: No stable timeline for drug approval (12-24 months with conflicting overlaps)
 Egypt	82	<ul style="list-style-type: none"> Supply chain vulnerability: Foreign currency constraints that delays imports; possible cold storage risks Manufacturing risk: Government's pharma ingredient purchase is a potential roadblock to future operations

Site Screening | Sites from select countries are shortlisted based on set criteria to enable strong engagement and speedy trial completion

We will activate the RESI Phase III trial sites in three strategic waves, with different group of sites in each wave

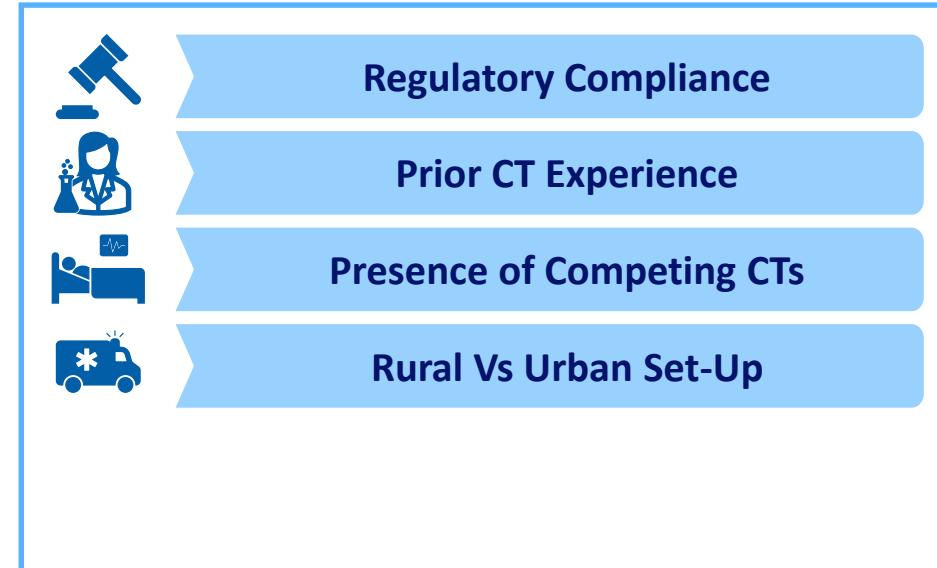
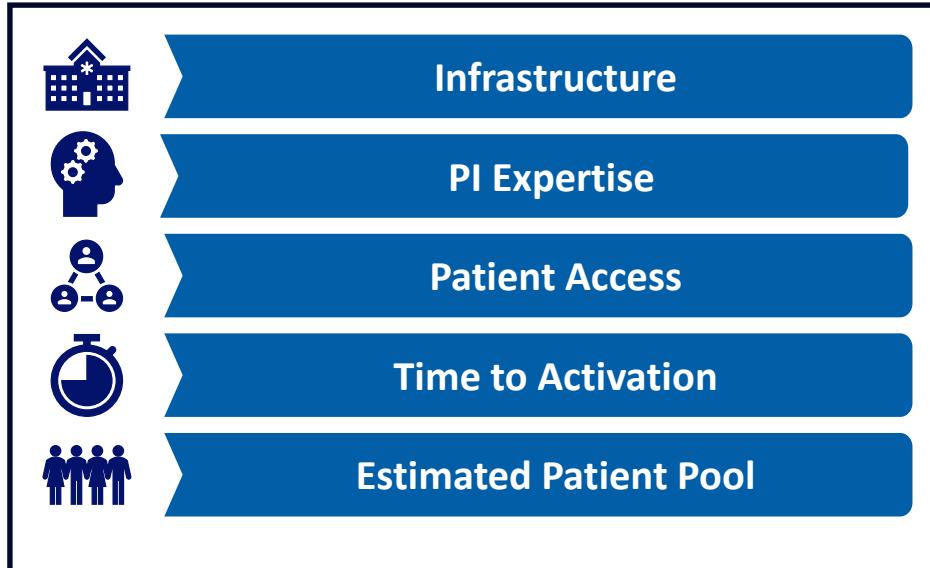
CRITERIA

Primary Factors

Evaluates to select sites for 3 waves

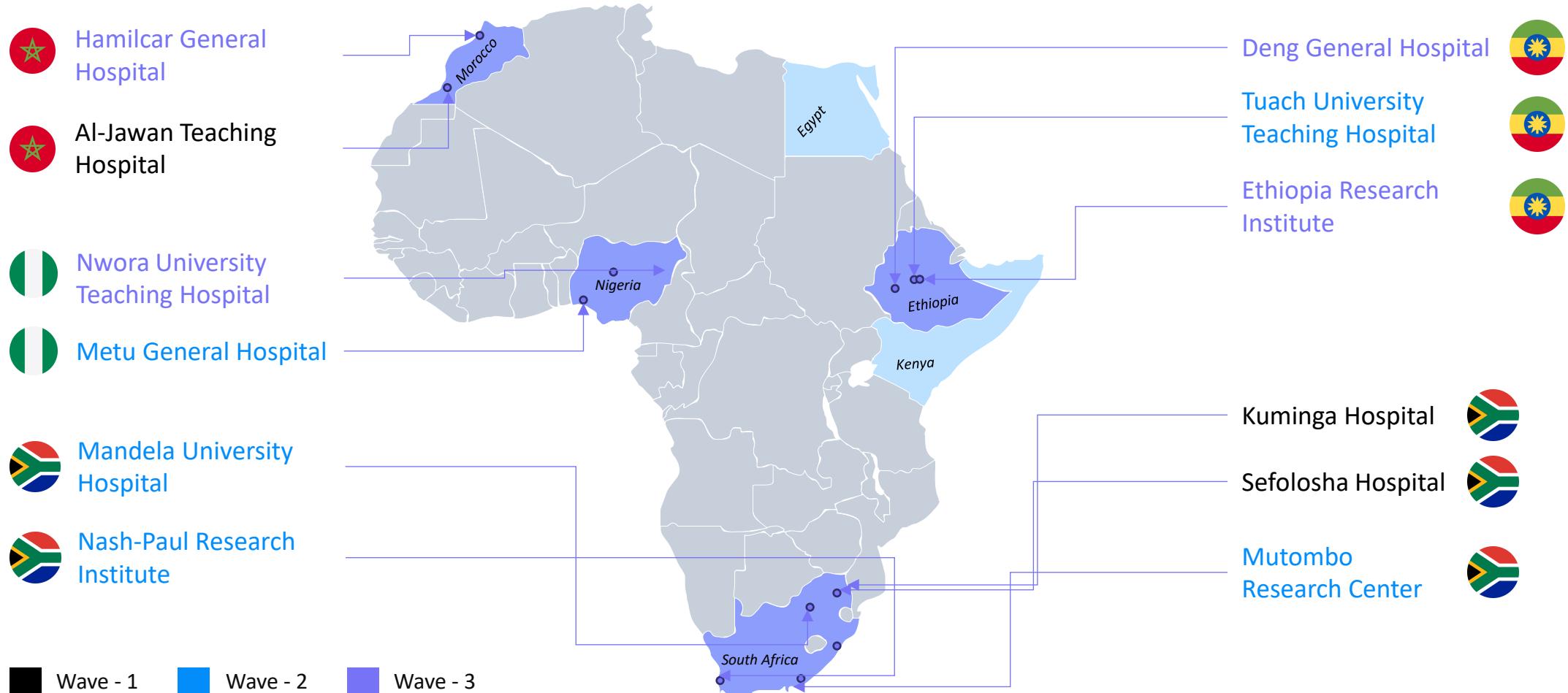
Secondary Factors

Evaluates to select sites within each wave



1. Site criteria matrix includes Infrastructure, PI Expertise and Patient Access with each metric scored out of 5

Site Screening | This portfolio balances fast activation, high patient pools, & geographic diversity enabling ~600 patient enrollment



Prioritization emphasizes sites with quality scores $\geq 11/15$, activation timelines ≤ 180 days, and minimal conflicts, aligning with MARA's mission for efficient, ethical trials

Wave -1 sites | Selected to achieve ‘first-patient-in’ as quickly as possible to establish trial momentum

All the sites were selected for their low activation time of **30-60 days for rapid startup** of trial sites



Site Name	Patient Pool ¹	Quality Score ²	Key Strengths
Sefolosha Hospital	16 - 48	13/15	<ul style="list-style-type: none"> Regulatory compliance: High Excellent patient access with rural community Prior CT experience: Yes, TB experience
Kuminga Hospital	32 - 48	8/15	<ul style="list-style-type: none"> Operational feasibility: Urban location aids logistics Prior CT experience: Yes, DR-TB trials
Al-Jawan Teaching Hospital	0 - 16	13/15	<ul style="list-style-type: none"> Prior CT experience: Yes Regulatory compliance: Prioritized for Morocco's regulatory maturity and international distribution pathways

1. Estimated patient pool assuming 80% enrollment rate; 2. Quality score calculated based on Infrastructure, PI Expertise, Patient Access in site matrix

Wave -2 sites | Selected to bring in volume to meet patient enrollment target

All the sites were selected for the high-quality infrastructure and high patient volume



Site Name	Patient Pool ¹	Quality Score ²	Key Strengths
Mandela University Hospital	40 - 80	13/15	<ul style="list-style-type: none"> Quality driver: High-volume, high-quality "anchor" site that is reliable and expected to be a top enroller for the entire trial
Mutombo Research Center	32 - 64	10/15	<ul style="list-style-type: none"> Location: High-quality rural site to mitigate the risk of urban site saturation
Nash-Paul Research Institute	40 - 80	12/15	<ul style="list-style-type: none"> High volume site with dedicated capacity Presence of competing trials: No, patient pool focused on RESI trial
Tuach University Teaching Hospital	16 - 64	15/15	<ul style="list-style-type: none"> Quality driver: Best-in-class center, most well-balanced site in the entire portfolio Presence of competing trials: Yes, but offset by higher patient pool
Metu General Hospital	20 - 40	9/15	<ul style="list-style-type: none"> Location: Urban (Lagos) site that mitigates the known risk of transportation delays in rural Nigeria

1. Estimated patient pool assuming 80% enrollment rate; 2. Quality score calculated based on Infrastructure, PI Expertise, Patient Access in site matrix

Wave -3 sites | Selected for contingency planning and strategic advantages

All the sites were selected to secure upper end of patient target and build Mara's future footprint



Site Name	Patient Pool ¹	Quality Score ²	Key Strengths
Deng General Hospital	16 - 40	11/15	<ul style="list-style-type: none"> A high-quality secondary site in Ethiopia. Activated in Wave 3 to build on partner CRO experience and help secure the final patient numbers
Nwora University Teaching Hospital	40 - 80	12/15	<ul style="list-style-type: none"> A high-volume, high-infrastructure site. It is placed in Wave 3 specifically to allow time to mitigate its known high-risk factor: "Slow EC turnaround"
Ethiopia Research Institute	32 - 64	10/15	<ul style="list-style-type: none"> The site has excellent facilities but "limited to no CT experience". It is included so MARA can "up-skill staff" and build a future-capable partner
Hamilcar General Hospital	0 - 16	11/15	<ul style="list-style-type: none"> Existing Mara relationship: The site has previous MARA experience in virology Prior CT experience: Yes Strong patient accessibility

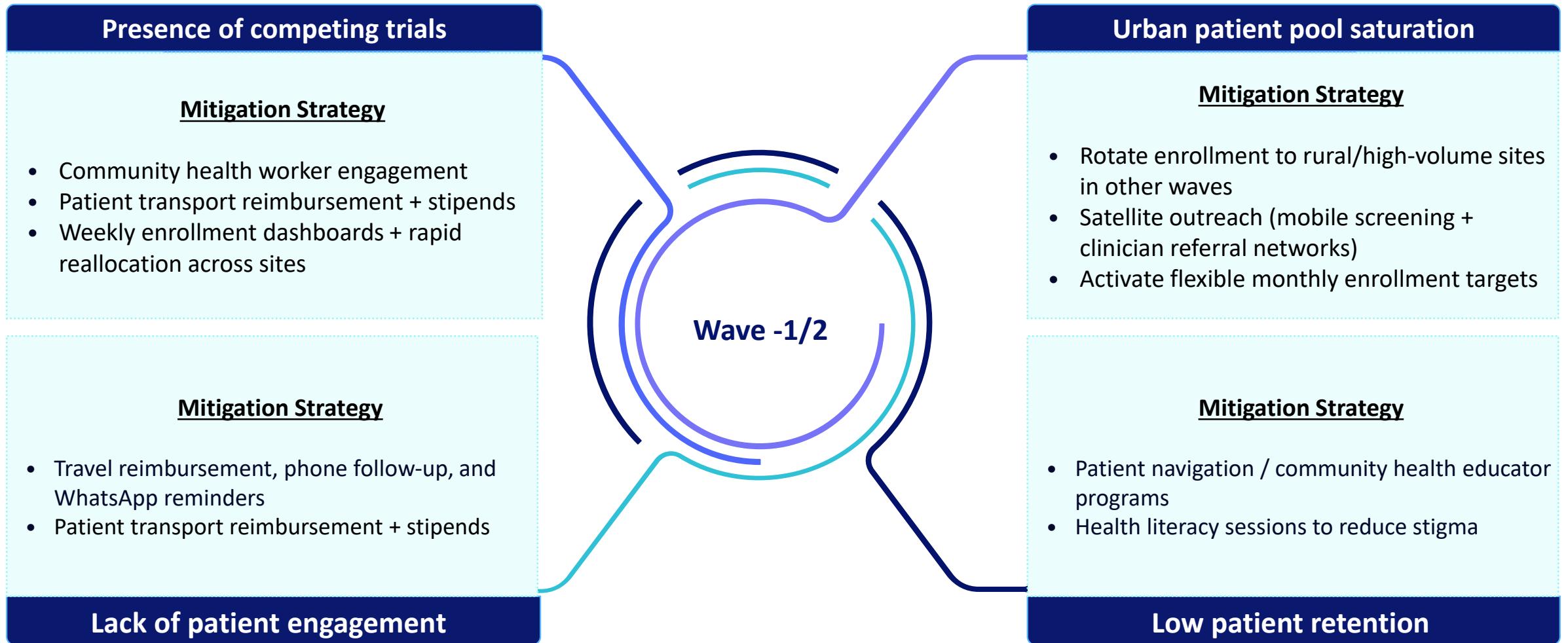
1. Estimated patient pool assuming 80% enrollment rate; 2. Quality score calculated based on Infrastructure, PI Expertise, Patient Access in site matrix



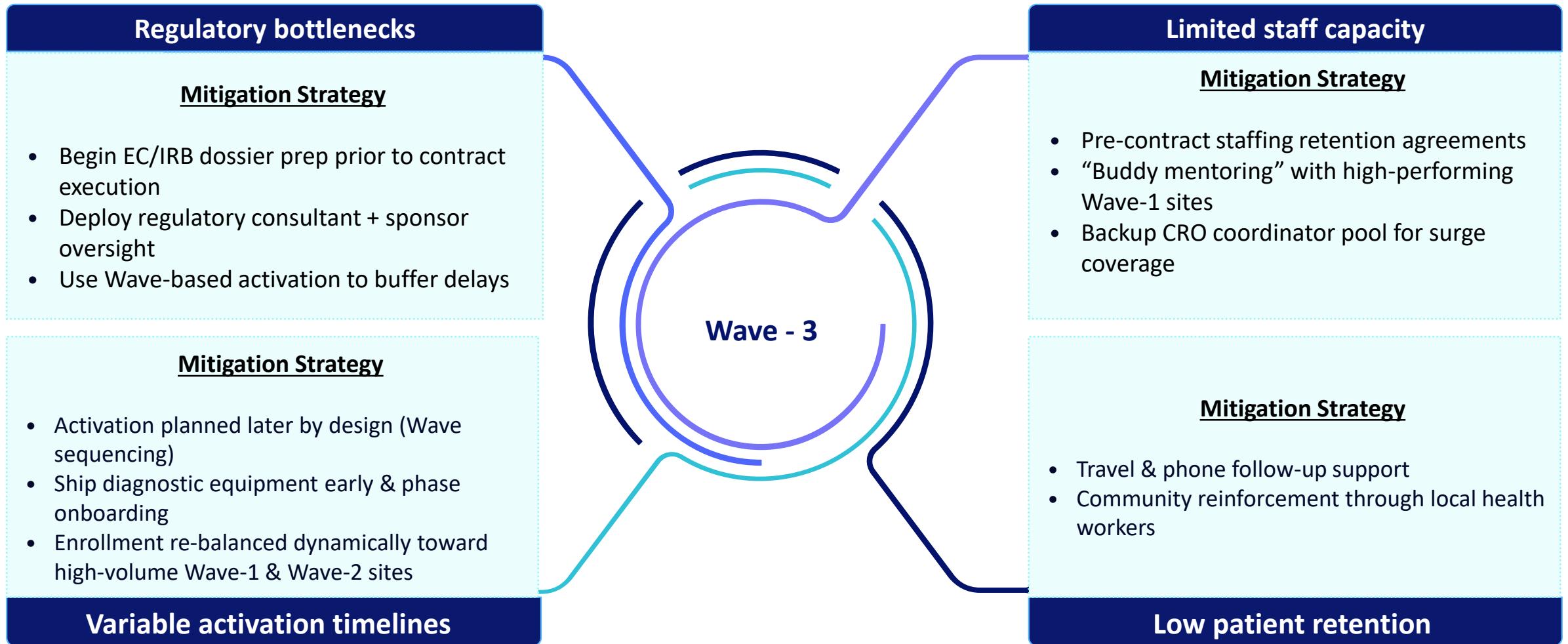
Protecting What Matters

Risk Mitigation Strategy

Ensuring patient enrollment and trial continuity are the key priorities for sites in wave 1 and 2



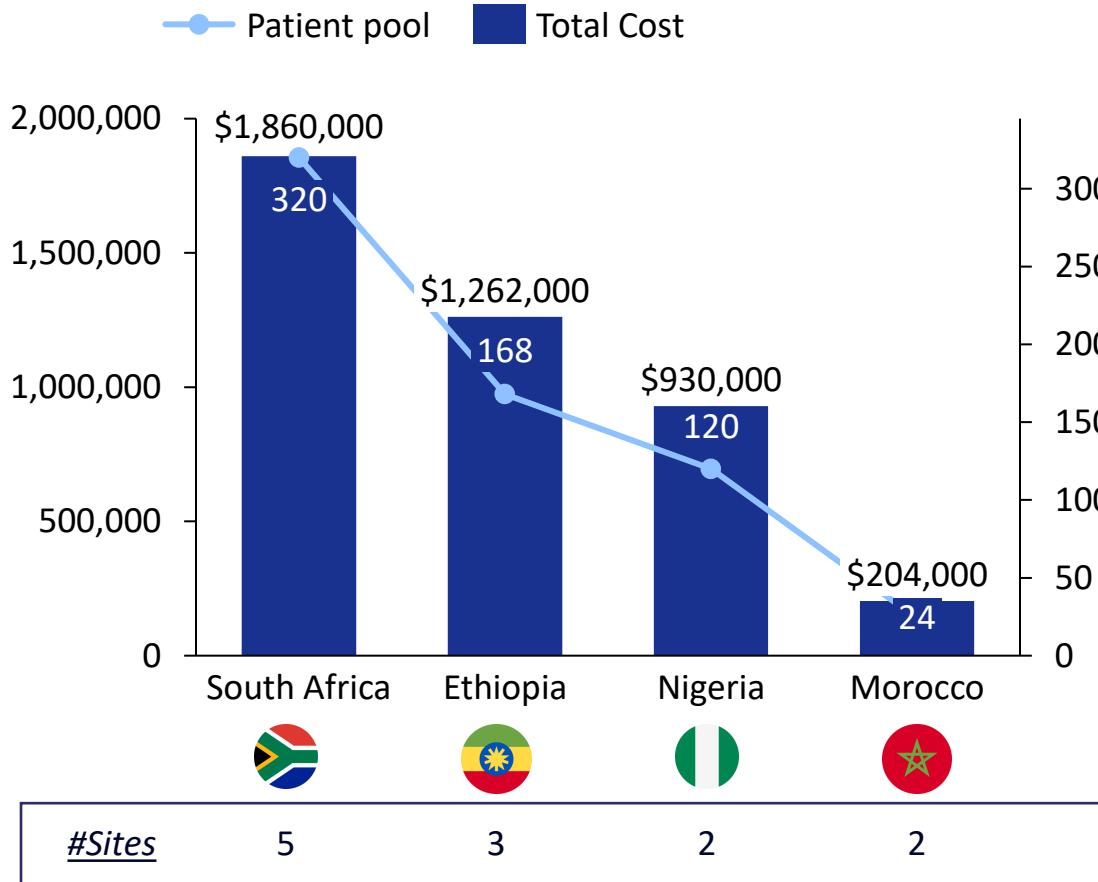
Overcoming slow regulatory turnaround, capacity constraints and activation timeline are the key priorities for sites in wave – 3



~70% of budget is allocated for South Africa and Ethiopia to capture high patient pools



Total budget estimate for phase-III RESI Trial (\$4,256,000)



[South Africa](#) (44%): Early patient enrollment driver
Cost per patient: \$5,812



[Ethiopia](#) (30%): Strategic scale-up region
Cost per patient: \$7,511



[Nigeria](#) (22%): Strategic scale-up region
Cost per patient: \$7,750



[Morocco](#) (4%): Regulatory stability anchor
Cost per patient: \$8,500

Strategic value: manufacturing and distribution hub to expedite global commercialization

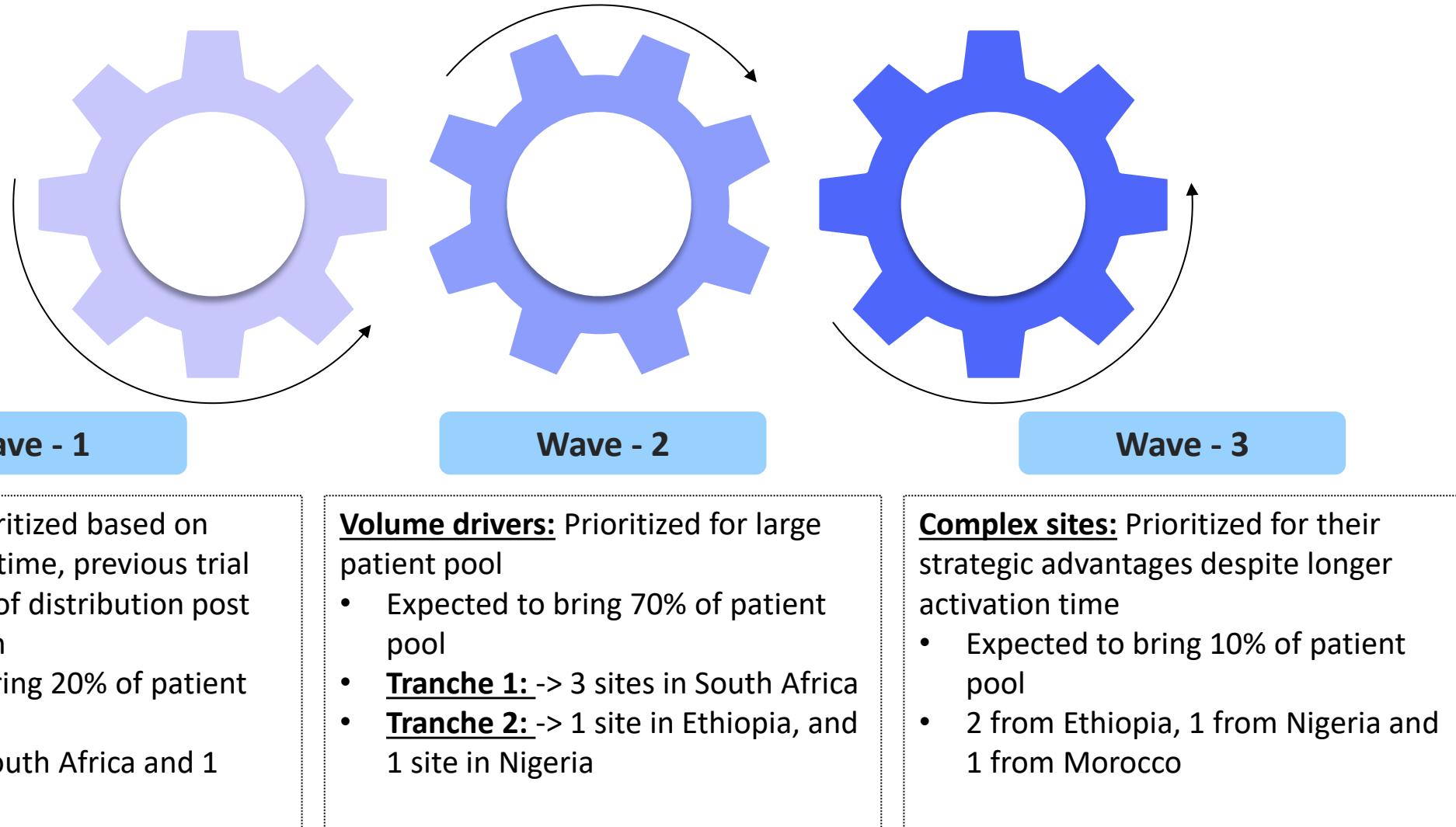
Note: Detailed cost breakdown for each country in the Appendix; Total costs include fixed cost and variable cost; Fixed Cost per Site includes activation, regulatory, training, monitoring expenses; Variable Cost per Patient includes enrollment and follow-up from 80% pool

Every Moment Counts When Lives are at Stake

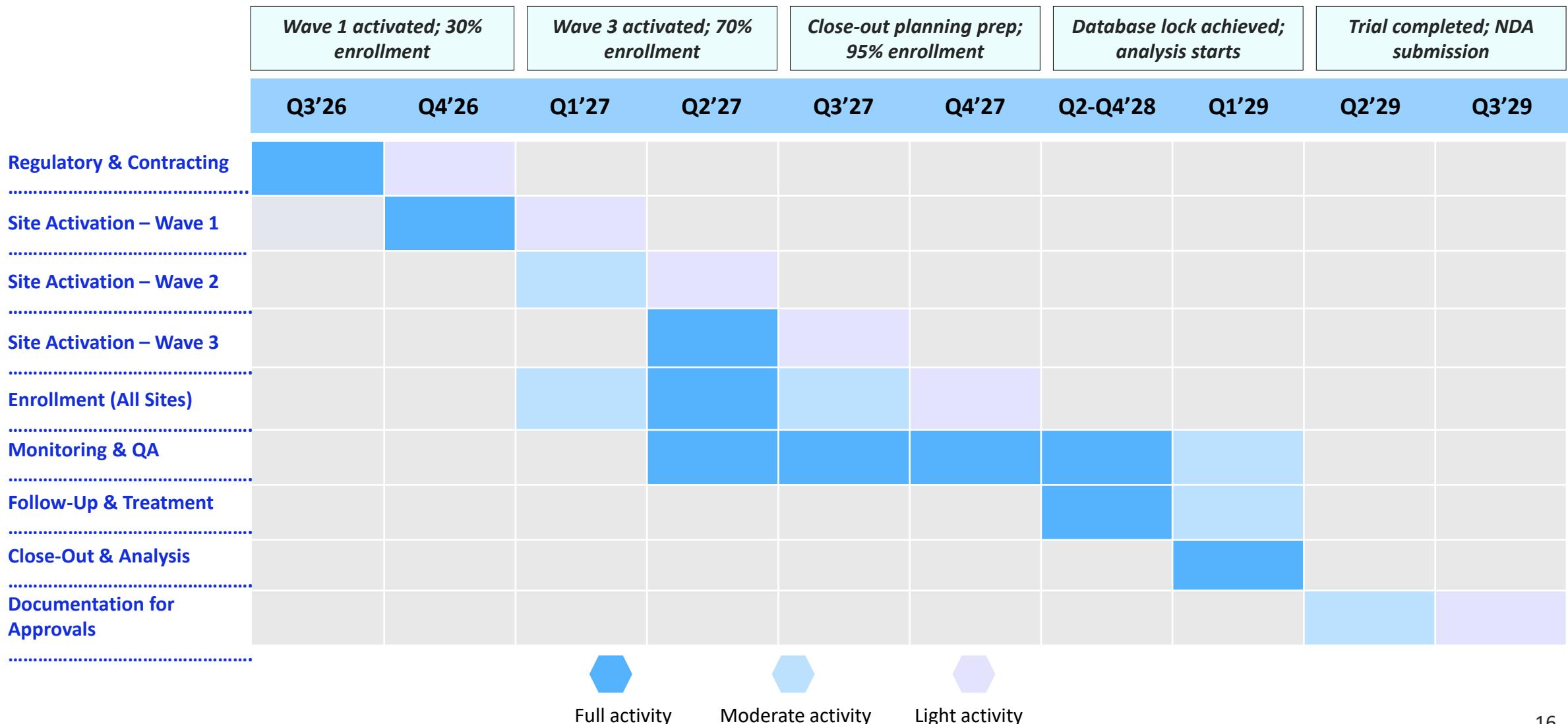
Clinical Trial Projected Timeline



RESI phase III trial sites should be based on phased activation to mitigate enrollment risk and enable speed to market



RESI phase III trial would require 2 years for completion, from site activation in Q4'26 to final database lock in Q1'2029





Appendix

Risk Mitigation | Protection of Enrollment & Maintaining Trial Continuity (Wave- 1)



Risk Area	Where This Risk Appears	Impact on Trial	Mitigation Strategy (What We Will Do)	Ownership
Competing Trials / Patient Competition	Sefolosha Hospital	<ul style="list-style-type: none"> Lower enrollment pace Longer recruitment cycles 	<ul style="list-style-type: none"> Community health worker engagement Patient transport reimbursement + stipends Weekly enrollment dashboards + rapid reallocation across sites 	Site PI + Enrollment Manager
Urban Patient Pool Saturation	Al-Jawan Teaching Hospital, Mutombo Research Center	<ul style="list-style-type: none"> Fast early enrollment followed by plateau 	<ul style="list-style-type: none"> Rotate enrollment to rural/high-volume sites in Wave 2 & Wave 3 Satellite outreach (mobile screening + clinician referral networks) Activate flexible monthly enrollment targets 	CRO Feasibility Lead + Site PI
Patient Engagement & Retention Risk	All Wave- 1 Sites (urban communities)	<ul style="list-style-type: none"> Loss-to-follow-up impacting primary endpoint 	<ul style="list-style-type: none"> Travel reimbursement, phone follow-up, and WhatsApp reminders Patient navigation / community health educator programs Health literacy sessions to reduce stigma 	Site Coordinator + Community Health Teams

Risk Mitigation | Protection of Enrollment & Maintaining Trial Continuity (Wave- 2)



Risk Area	Where This Risk Appears	Impact on Trial	Mitigation Strategy (What We Will Do)	Ownership
Competing Trials / Patient Competition	Tuach University Teaching Hospital, Sefolosha Hospital, Metu General Hospital	<ul style="list-style-type: none"> Lower enrollment pace Longer recruitment cycles 	<ul style="list-style-type: none"> Recruitment incentives Community health connectors Active weekly re-balancing of enrollment targets 	Site PI + Enrollment Manager
Urban Patient Pool Saturation	Metu General Hospital	<ul style="list-style-type: none"> Plateau may occur late in study 	<ul style="list-style-type: none"> Overflow routing to rural Wave-3 centers Local clinician referral networks 	CRO Feasibility Lead
Patient Engagement & Retention Risk	All Wave- 2 Sites (mixed rural/urban)	<ul style="list-style-type: none"> Missed follow-ups & endpoint variance 	<ul style="list-style-type: none"> Transport support + messaging reminders Engage community leaders to reduce stigma 	Site Coordinator + Community Health Teams

Risk Mitigation | Protection of Enrollment & Maintaining Trial Continuity (Wave- 3)



Risk Area	Where This Risk Appears	Impact on Trial	Mitigation Strategy (What We Will Do)	Ownership
Slow Ethics / Regulatory Turnaround	Nwora University Teaching Hospital, Ethiopia Research Institute	<ul style="list-style-type: none"> Delayed site activation Delayed first-patient-in 	<ul style="list-style-type: none"> Begin EC/IRB dossier prep prior to contract execution Deploy regulatory consultant + sponsor oversight Use Wave-based activation to buffer delays 	CRO Regulatory Lead + Site Admin
Limited Staff Capacity / Turnover Risk	Nwora University Teaching Hospital, Deng General Hospital, Ethiopia Research Institute, and Hamilcar General Hospital (Wave-3 sites)	<ul style="list-style-type: none"> Operational slowdowns Inconsistent data quality Extended enrollment timelines 	<ul style="list-style-type: none"> Pre-contract staffing retention agreements “Buddy mentoring” with high-performing Wave-1 sites Backup CRO coordinator pool for surge coverage 	Clinical Ops Lead + CRO PM
Variable Activation Timelines	Ethiopia Research Institute, Deng General Hospital	<ul style="list-style-type: none"> Late site contribution to total patient targets 	<ul style="list-style-type: none"> Activation planned later by design (Wave sequencing) Ship diagnostic equipment early & phase onboarding Enrollment re-balanced dynamically toward high-volume Wave-1 & Wave-2 sites 	Sponsor + CRO Launch Team
Patient Engagement & Retention Risk	Particularly Deng General Hospital and rural catchment sites	<ul style="list-style-type: none"> High loss-to-follow-up impacting primary endpoint 	<ul style="list-style-type: none"> Travel & phone follow-up support Community reinforcement through local health workers 	Site Coordinator + Community Health Teams 19

Sites | Key Risks and Mitigation Strategies

Site	Country	Key Risks	Mitigation Strategies
Kuminga Hospital	South Africa	<ul style="list-style-type: none"> Weak infrastructure Limited capacity 	<ul style="list-style-type: none"> Assess infrastructure & budget for upgrades Leverage prior DR-TB trial experience Ensure diagnostic readiness
Mandela University Hospital	South Africa	<ul style="list-style-type: none"> Staffing constraints, urban competition long activation (45–105 days) large patient pool (50–100) multiple competing trials 	<ul style="list-style-type: none"> Negotiate staffing & retention upfront Add dedicated trial staff Start early recruitment discussions Implement backup staffing/contract nurses
Nash-Paul Research Institute	South Africa	<ul style="list-style-type: none"> Limited CT experience Inexperienced team 	<ul style="list-style-type: none"> Provide GCP/protocol training Deploy experienced CRO oversight Start with conservative enrollment Pair with an experienced site for mentorship
Sefolosha Hospital	South Africa	<ul style="list-style-type: none"> Overlapping TB trial Rural location Patient pool competition 	<ul style="list-style-type: none"> Offer differentiated patient support Weekly monitoring & backup sites Leverage PI expertise & community recruitment
Mutombo Research Center	South Africa	<ul style="list-style-type: none"> Rural location, moderate ratings Bureaucratic delays Patient pool National EC oversight 	<ul style="list-style-type: none"> Transport & telemedicine support Leverage EC relationships Validate patient catchment & mobile diagnostics Build on previous trial experience

Sites | Key Risks and Mitigation Strategies

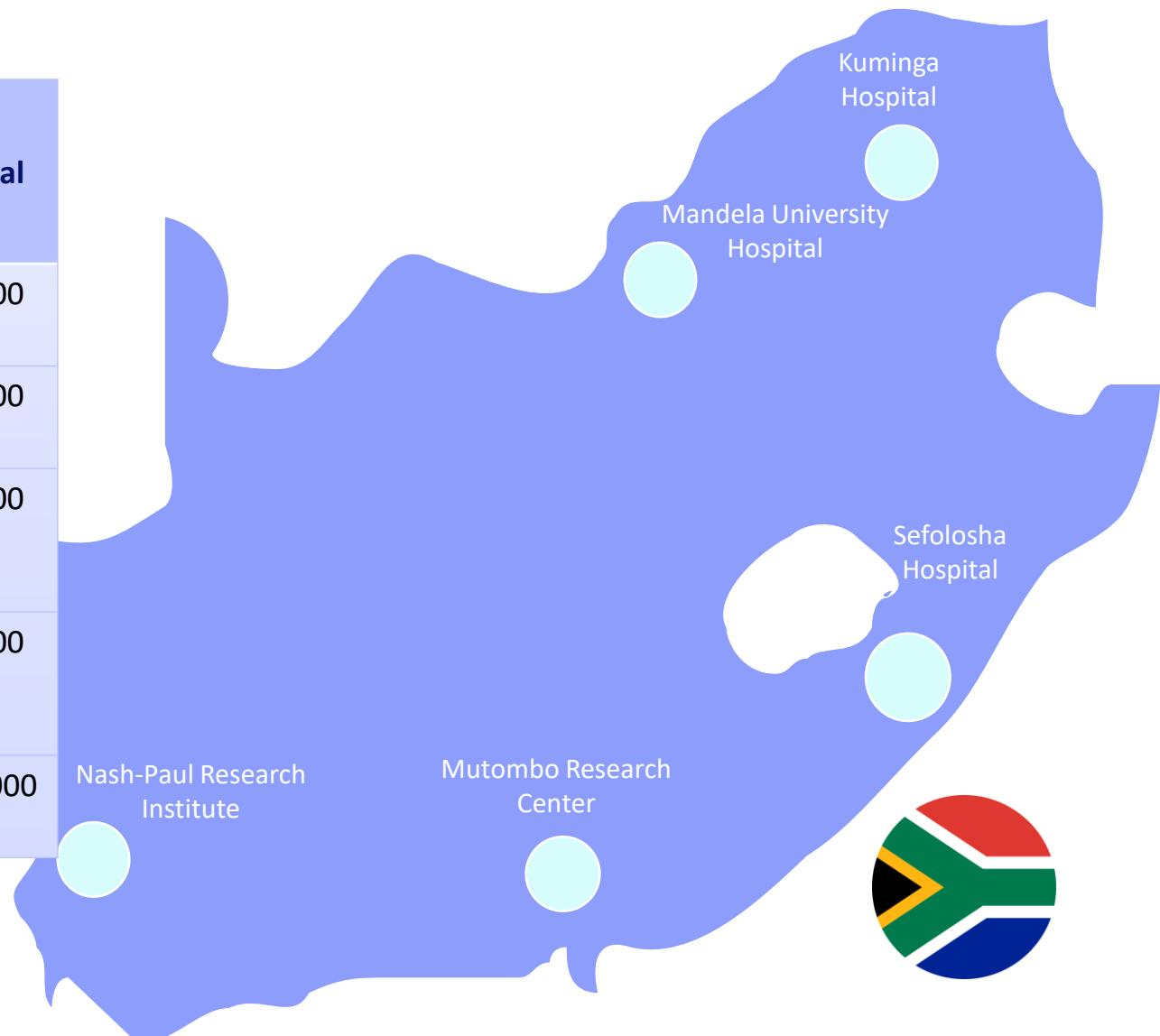
Site	Country	Key Risks	Mitigation Strategies
Al-Jawan Teaching Hospital	Morocco	<ul style="list-style-type: none"> Previous TB trial had data quality concerns Small patient pool (0–20) in urban Agadir Fast activation (30–90 days) may not allow proper setup Morocco's strict regulatory environment 	<ul style="list-style-type: none"> Root cause analysis & enhanced monitoring Data management training & dedicated monitor Use EDC with validation rules Consider probationary enrollment & exclusion if issues severe
King Hassan II Medical Center	Morocco	<ul style="list-style-type: none"> Very small patient pool (0–10) – enrollment Requires GCP and regulatory guidance 	<ul style="list-style-type: none"> Engage community networks & broad catchment Provide transportation support Satellite/outreach approach with urban site partnership
Nwora University Teaching Hospital	Nigeria	<ul style="list-style-type: none"> MD staffing concerns – high turnover likely Long activation (90–180 days) Urban Abuja – competitive environment 	<ul style="list-style-type: none"> Early EC submission & staff contract commitments Hire dedicated MDs & provide retention packages Use an experienced CRO; backup staffing & monthly monitoring
Metu General Hospital	Nigeria	<ul style="list-style-type: none"> Urban Lagos – highly competitive Moderate activation (60–150 days) with high variability 	<ul style="list-style-type: none"> TB/ID protocol training Leverage virology trial relationships Partner with experienced sites & regular monitoring
Tuach University Teaching Hospital	Ethiopia	<ul style="list-style-type: none"> Competing MDR-TB trial ongoing Long activation (90–120 days) Large patient pool (20–80) split with competitor 	<ul style="list-style-type: none"> Competitive analysis & exclusive enrollment windows Patient support/stipends Leverage university reputation Monitor competitor enrollment & differentiate trial benefits

Sites | Key Risks and Mitigation Strategies

Site	Country	Key Risks	Mitigation Strategies
Ethiopia Research Institute	Ethiopia	<ul style="list-style-type: none"> • No prior inspection • No CT experience • Inexperienced staff • Large patient pool (40–80) 	<ul style="list-style-type: none"> • Consider exclusion unless strategic • Full-time CRO training & staged activation • PI & staff GCP training • Start with qualification/feasibility phase & intensive monitoring
Deng General Hospital	Ethiopia	<ul style="list-style-type: none"> • Long activation (90–180 days) • Specialized equipment unavailable • Suburban location 	<ul style="list-style-type: none"> • Pre-qualify & budget for equipment • Consider leasing/provision by sponsor • Staff training & validate maintenance • Possible 3–6 month enrollment delay

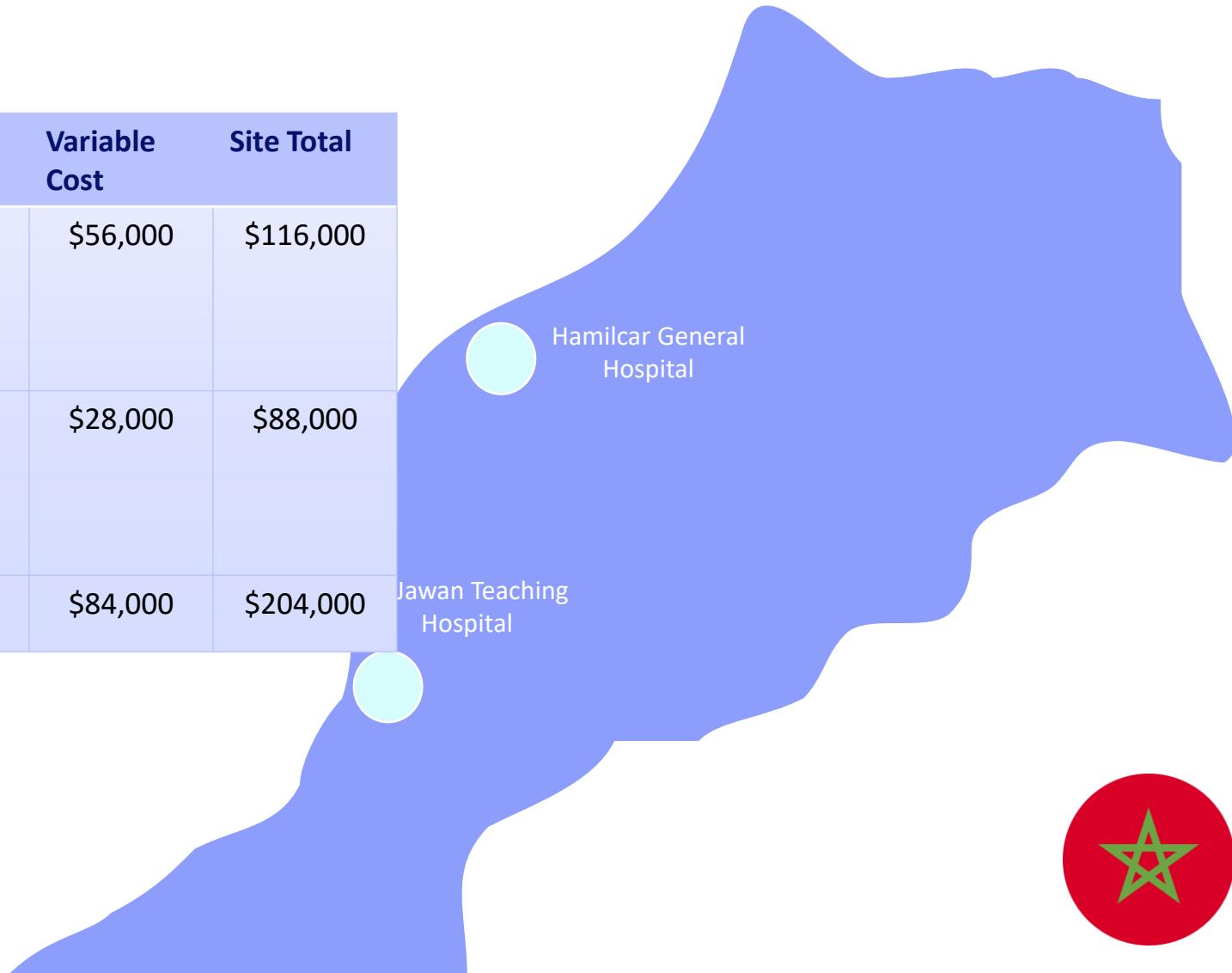
Budgeting | South Africa

Site Name	Wave	Midpoint Patients	Fixed Cost	Variable Cost	Site Total
Sefolosha Hospital	1	32	\$150,000	\$224,000	\$374,000
Kuminga Hospital	1	40	\$150,000	\$280,000	\$430,000
Mandela University Hospital	2, P1	60	\$150,000	\$420,000	\$570,000
Mutombo Research Center	2, P1	48	\$150,000	\$336,000	\$486,000
Subtotal	-	180	\$600,000	\$1,260,000	\$1,860,000



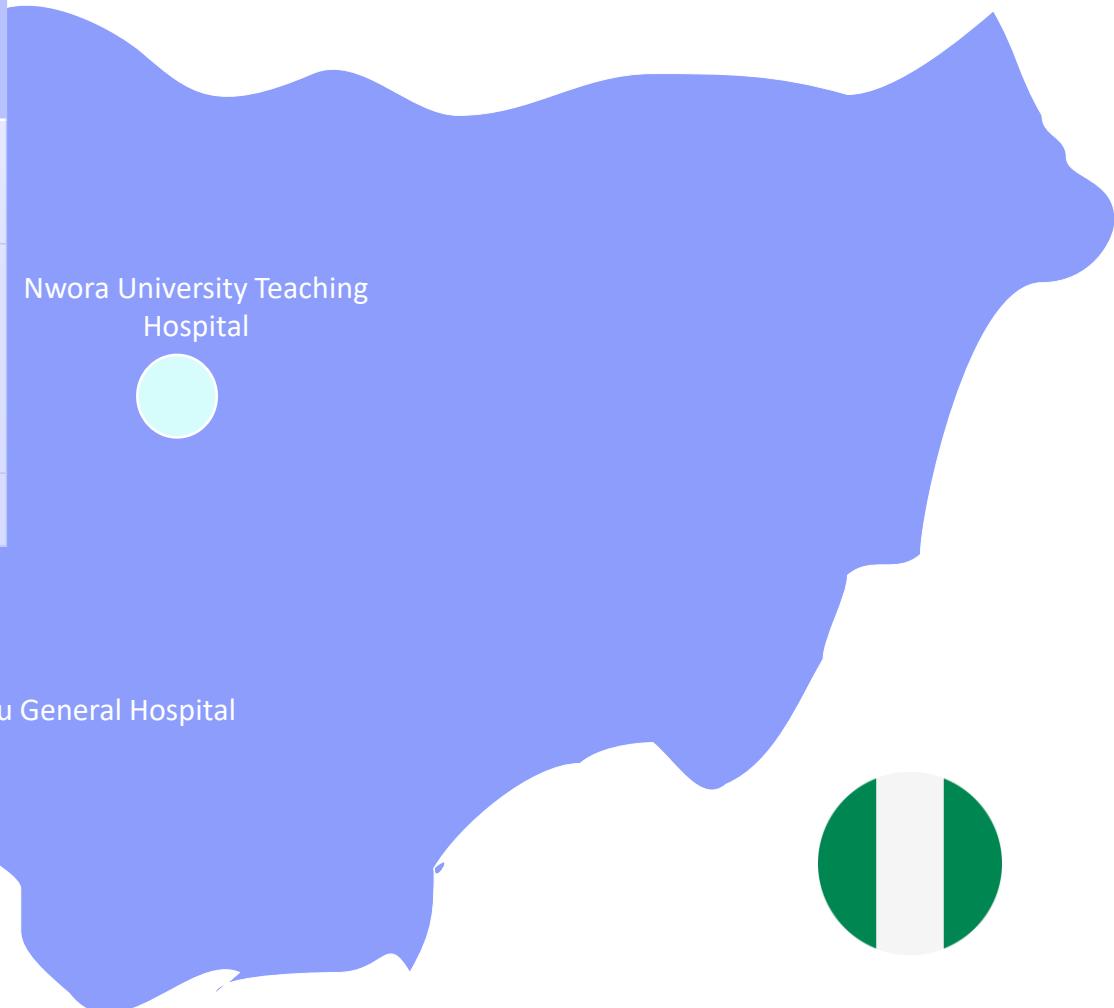
Budgeting | Morocco

Site Name	Wave	Midpoint Patients	Fixed Cost	Variable Cost	Site Total
Al-Jawan Teaching Hospital	1	8	\$60,000	\$56,000	\$116,000
Hamilcar General Hospital	2, P2	4	\$60,000	\$28,000	\$88,000
Subtotal	-	12	\$120,000	\$84,000	\$204,000



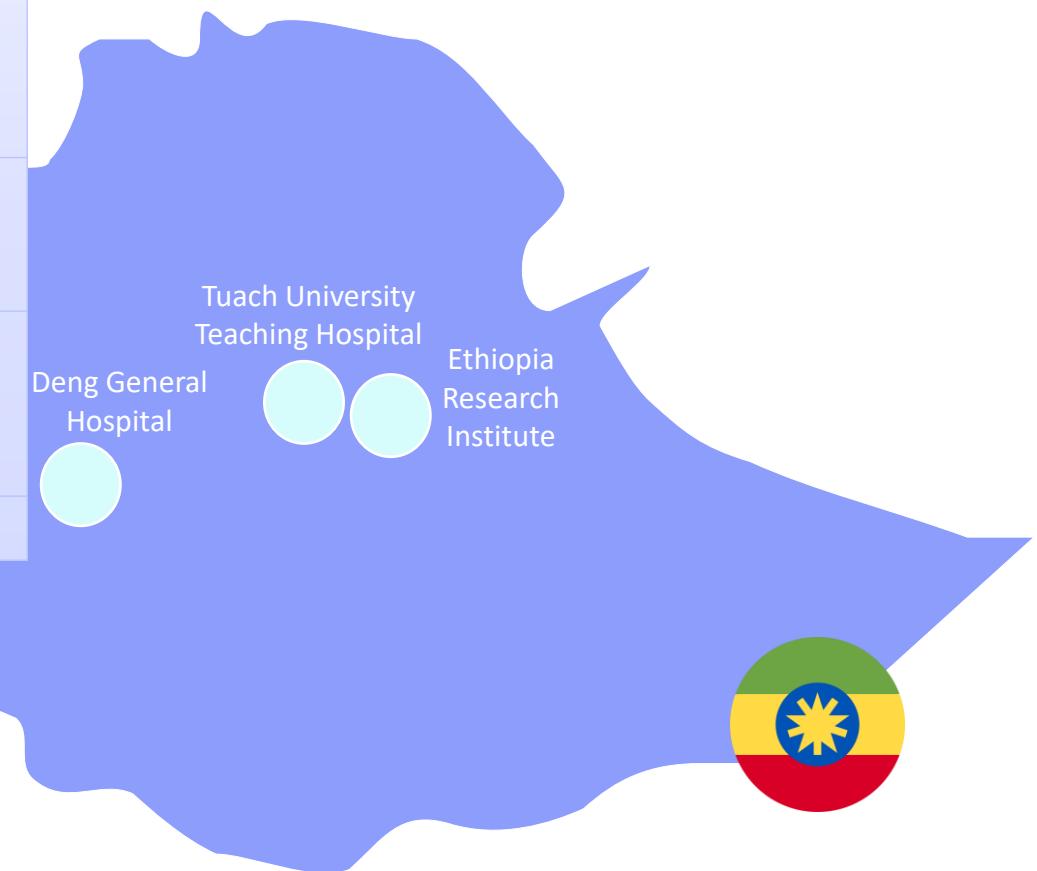
Budgeting | Nigeria

Site Name	Wave	Midpoint Patients	Fixed Cost	Variable Cost	Site Total
Metu General Hospital	2, P2	30	\$150,000	\$210,000	\$360,000
Nwora University Teaching Hospital	3	60	\$150,000	\$420,000	\$570,000
Subtotal	-	90	\$300,000	\$630,000	\$930,000



Budgeting | Ethiopia

Site Name	Wave	Midpoint Patients	Fixed Cost	Variable Cost	Site Total
Tuach (Tosh) University Teaching Hospital	2, P2	40	\$150,000	\$280,000	\$430,000
Deng General Hospital	3	28	\$150,000	\$196,000	\$346,000
Ethiopia Research Institute	3	48	\$150,000	\$336,000	\$486,000
Subtotal	-	116	\$450,000	\$812,000	\$1,262,000



RESI phase III trial would require 2 years for completion, from site activation in Q4'26 to final database lock in Q1'2029

