WHO WE ARE & WHAT WE DO

CLINICAL RESEARCH
Clinical Research

Aurum’s work spans the cascade of health care from innovation to implementation, as illustrated below:

Our Model: Bridging the worlds of research, policy and implementation for impact

The Aurum Institute has conducted over 60 randomized clinical trials (RCTs) and socio-behavioural studies in the past two decades, focusing on:

1. HIV vaccines, treatment and prevention, including oral, topical, and long-acting injectable Pre-exposure Prophylaxis (PrEP)
2. TB treatment, host-directed therapy, vaccines, preventative therapy and diagnostics
3. SARS-CoV-2 vaccines and treatment

Aurum’s distinct strength is the collective scientific, operational and management experience of its research leadership, and its high-functioning resources, systems and processes to effectively implement large-scale complex clinical trials. Capabilities in this context include:

- Established community and stakeholder relationships
- Demonstrated success in identifying, recruiting and retaining diverse African volunteer populations, including high- and low-risk populations for HIV and TB studies (adults, adolescents, men who have sex with men (MSM) and female sex workers (FSW))
- Specialized and routine laboratory and clinical facilities and capabilities
- Cross-site innovations and technology
- Strong institutional support, with highly trained and experienced administrative, technical and operations staff

Aurum has a proven track record of managing multiple studies across several countries, with research partnerships in South America, India, Southeast Asia and other sub-Saharan African countries. In 2020, it was awarded a seven-year grant by the National Institutes of Health (NIH) for a Clinical Trials Unit (CTU) to drive the scientific agendas of the HIV Vaccine Trials Network (HVTN) and the AIDS Clinical Trials Group (ACTG). The CTU uses Aurum’s collective research infrastructure, experience, and scientific understanding of biological, behavioural, and structural risks to advance new and proven HIV, TB and COVID prevention and treatment options.

1Thibela TB (20 sites in 1 country), TB Sequel (4 sites in 4 countries), WHIP3TB (8 sites in 3 countries), XTEND (20 sites in 1 country), Aurum102/THYB05 (2 sites in 2 countries), AS300B/I2003B/PHONEIx (27 sites in 12 countries)
A. Our Technical Expertise

1. Clinical Research Sites
The Aurum Institute has four Clinical Research Sites (CRS) in South Africa with the resources and infrastructure to conduct clinical trials effectively and safely.

a. Klerksdorp CRS, North West Province: The Klerksdorp CRS is located in a peri-urban area and has three separate research clinics, a research laboratory and pharmacy. Its layout is configurable for various trial designs and for multiple, concurrent studies. The site has been operating since 2005 and been a DAIDS-funded core site since 2006. It has conducted 31 trials and studies, 19 of which were randomized clinical trials (RCTs) (12 DAIDS-funded), screening >7,500 persons, and enrolling >3,000 participants. The site has specialised capabilities for geospatial mapping to identify recruitment hot spots, and for mucosal sampling and processing.

b. Rustenburg CRS, North West Province: The Rustenburg CRS is conveniently located in the Rustenburg city centre. Facilities include an Adult Clinic and an Adolescent & Youth Friendly Services (AYFS) Clinic, a research laboratory and pharmacy. The site has been operating 2008 and was registered as a DAIDS protocol-specific site in 2016. It has successfully implemented 22 trials and studies, seven of which were RCTs (three DAIDS-funded), screening >15,500, and enrolling >5,100 participants. It has mucosal sampling and processing capabilities.

c. Tembisa CRS, Gauteng Province: The Tembisa CRS is ideally situated on the grounds of the Tembisa Provincial Tertiary Hospital in the urban township of Tembisa. The site operates four separate clinics with capacity to conduct large-scale, concurrent studies, and a research laboratory and pharmacy. The site has been operating since 2008 and been a DAIDS protocol site since
2015. It has conducted 21 trials and studies, 17 of which were RCTs (five DAIDS-funded), screening >3,700 and enrolling >2,100 participants. It has specialised capabilities for spirometry and six-minute walk assessments.

**d. Pretoria CRS, Gauteng Province:** The Pretoria CRS (Previously Vx Pharma) was acquired by Aurum in 2020. It is located in The Enterprise Building of the Innovation Hub where clinical trials have been conducted since 2014. Aurum Pretoria CRS comprises an outpatient section as well as an inpatient area that includes a ward with 23 beds.

Aurum’s sites in the North West also provide cold-chain storage for COVID vaccines in support of the South African national rollout programme.

### 1.1. Staffing

The Clinical Research Division is led by a Managing Director supported by a Director of Operations and a Clinical Director, and by heads of department for Research Programmes, Quality, Data, Pharmacy, Laboratory and Community services.

Each CRS has a dedicated, full-time CRS Leader/Principal Investigator (PI) who is an experienced research physician. CRS teams are trained on sponsor/network requirements, regulatory standards, Good Clinical / Laboratory / Pharmacy Practice (GCP, GCLP, GPP) as appropriate and individual protocol requirements.

**Teams are cross-trained to work on multiple protocols at a time.**

See Annexure 1 for detail on the CRS Staffing Structure

### 1.2. Infrastructure and Basic Services

Klerksdorp, Rustenburg and Tembisa have the following infrastructure and basic services:

**Electrical Supply:** In the event of power disruptions, generators supply back-up power to the entire facility to avoid temperature deviations and equipment failure. Generators are tested weekly and serviced every three months. Uninterrupted Power Supply units (UPSs) are connected to fridges, freezers, and centrifuges, and ultra-low freezers are connected to CO2 in case of compressor failure.

**Security:** All areas, including pharmacies and laboratories, are access-controlled with additional security gates and burglar bars. An out-sourced security company provides 24-hour

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Division of AIDS (DAIDS), formed in 1986 by the US National Institutes of Health to develop and implement an HIV research agenda.
guarded security, and there is an on-site alarm system linked to an armed response service.

**Information Technology (IT):** All computers are password protected and have antivirus software. CRSs are connected in a star topology WAN design, linked by fibre at 50Mbps, with redundancy microwave linkage at 20Mbps for back up. All CRSs are connected to the central data centre at 200Mbps, and internet security is assured by a central FortiGate firewall. IT support is outsourced to DataCentrix (datacentrix.co.za).

**Vehicles:** Each CRS has a fleet of vehicles allocated that are used for community education, recruitment, and retention (Klerksdorp and Rustenburg have four vehicles each, and Tembisa has seven).

**Occupational Health and Safety (OHS):** Trained staff (first aid, evacuation coordinators and fire-fighters) are responsible for daily safety on site. CRSs (including laboratories and pharmacies) are equipped with fire extinguishers, fire blankets, spillage kits, personal protective equipment, eyewash stations, first aid boxes, and fire horns. OHS medical assessments (including Hepatitis B vaccination and chest X-rays) are provided for relevant staff, and HIV post-exposure prophylaxis is provided as per SOP.

**Infection Control:** All clinics have adequate ventilation with high ceilings and specifically designed ceiling fans to create an upward airflow to reduce and prevent transmission of airborne infections. Shielded ultraviolet germicidal irradiation (UVGI) devices are used in TB clinics to disinfect the area.

**Biohazardous Waste:** Disposal of biohazardous waste material is managed by the responsible staff in the clinical rooms, pharmacy, and laboratory as per OHS requirements. The appropriate color-coded disposal bins are used for general, biological, contaminated, sharp, and pharmaceutical material. The bins once full are sealed, removed, and stored in a safe and lockable designated area for collection by the contracted service provider for destruction by incineration. Certificates of destruction are filed.

**Temperature Monitoring and Control:** Room temperature is maintained at 15°C - 25°C in CRS pharmacies and laboratories, and monitored manually twice-daily using digital minimum/maximum thermometers.
Temperature and humidity are further monitored using Eltek® and/or Omniflex® continuous temperature monitoring systems, which send SMS notifications and emails to alert staff to any temperature excursions.

2. Clinical Research Services

a. Community Engagement
   All CRSs have strong relationships with community stakeholders and health providers, and have mature Community Advisory Boards (CABs) with representation from populations of interest. CAB members are educated on studies to be able to advise community stakeholders and potential study participants.

b. Recruitment and Retention
   Recruitment: Recruitment procedures follow the CRS Community Involvement Work Plan (CIWP) and the recruitment and retention SOP. Each study has an individual recruitment and enrolment plan, customised for the specific trial population in accordance with network/sponsor requirements. A Community Liaison Officer (CLO) and Recruitment/Retention team leaders at each CRS are responsible for educating and mobilising communities. Each protocol has a specific team allocated to conduct recruitment and retention. Community education materials (flyers, posters, leaflets etc.) are reviewed and approved by the Independent Ethics Committee. Accrual targets are monitored by the CRS Leader, CRS Coordinator, study coordinator and study investigator using a study-specific recruitment tracking log.

Study populations: Given the epidemiology of HIV and TB in the Klerksdorp, Rustenburg and Tembisa communities, the Aurum CRSs are well-positioned to implement both HIV and TB treatment and prevention studies. The CRSs have demonstrated access to TB-infected and uninfected persons for TB vaccine trials (prevention of disease and infection), and patients with drug-susceptible and drug-resistant TB for TB treatment, host-directed therapy, and therapeutic TB.

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1A BSL-3 laboratory is a state-of-the-art containment facility that enables the isolation and manipulation of organisms belonging to risk group three of infectious organisms, i.e. organisms with high individual risk but low community risk, such as drug-resistant TB. They are essential for research and proof-of-concept studies in developing new diagnostics or therapeutics.
vaccine trials. The CRSs works in close partnership with the Aurum Health Systems Strengthening Division (HSD), funded by the President’s Emergency Program for AIDS Relief (PEPFAR), to identify primary health clinics (PHCs) from which to recruit select study populations. Data is collected from the South African National HIV and TB databases (TIER.net and ETR.net), cleaned, and then visualized in geospatial or heat maps.

Retention: At the heart of the CRSs’ retention strategy is a commitment to a client-centred approach and continuous quality improvement to improve retention rates and participant experience. Multiple retention strategies and activities have been used successfully and may be modified as required for future studies.

c. Clinician Services

Standard of care: In addition to research clinical services, care is provided to participants at all CRSs for minor ailments, sexually transmitted infections (STIs), and contraception. The clinical team collaborates with Aurum’s Health Systems Strengthening Division to assist with patient initiation on ART, and is trained to manage medical emergencies.

Referral systems: CRSs contract with local specialist physicians and services as needed per protocol for services such as diagnostic radiology, obstetrics/gynaecology, paediatrics and ophthalmology.

- Klerksdorp has referral systems to 16 primary healthcare clinics (PHCs), and to the Klerksdorp Tshepong Hospital Complex across the road for emergency, chronic and specialised services.
- Rustenburg has referral pathways to 24 PHCs. The site is 1.4km from the JS Tabane Provincial Hospital and 1.3km from Life Peglerae private hospital for emergency and specialised services.
- Tembisa has established referral systems with 27 PHCs. The Tembisa Regional Hospital is situated on the same premises and has a 24-hour emergency service and a 10-bed adult intensive care unit. The CRS has links to nearby Zamokuhle Private Hospital for specialist services.

d. Research Pharmacy Services

Registration and compliance: Each CRS has a dedicated pharmacy designed and equipped in compliance with South African Pharmacy Council (SAPC) regulations and with international trial standards. They have DAIDS-approved pharmacy establishment plans to conduct study product management for HVTN and/or ACTG, and have been rigorously audited by SAHPRA, DAIDS, and various sponsor-contracted clinical research audit firms.

Research Pharmacy staff: A team of 12 SAPC-registered pharmacists and pharmacists’ assistants are cross-trained on research protocols, and have both blinded and open-label trial experience in administering investigational products to participants. They adhere to a
comprehensive set of standard operating procedures, maintain impeccable quality control and quality assurance standards, conduct internal audits between research sites, and share best practices for improvement.

**Pharmacy systems:** Pharmacies order study products using a web-based ordering system and use a paper-based DAIDS accountability log to account for all study products. Physical inventory checks of study products are conducted at least monthly and documented on the accountability log. Dispensing and preparation of products is initiated upon receipt of a valid protocol-specific prescription and labelled to ensure participant safety and confidentiality. A chain of custody log is signed by clinic staff upon collection of study products for administration to participants.

**Supply chain:** In Aurum’s role as lead investigator and study sponsor for large multicentre trials, the research pharmacy service also coordinates procurement and distribution of investigational products.

Aurum’s preferred logistics contractor, Pharma Logistics SA, partners with the SMO Group (now OXIMIO) to offer a global capability in:
- Procurement and comparator sourcing
- Import/export facilitation
- Storage and distribution at +15-25°C, +2-8°C, -20°C, -80°C and cryogenic temperatures

See Annexure 4 for Aurum’s Project Experience in Managing Investigational Products.

- Labelling/relabelling in compliance with Good Manufacturing Practice (GMP)
- Returns and destruction

**e. Research Laboratory Services**

Specimen testing and processing: CRS laboratories have on-site capability to perform the following:
- Serology – HIV rapid plasma reagin (RPR)
- Endocrinology – urine pregnancy
- Microbiology – urine microscopy, rapid trichomonas vaginalis and bacterial vaginosis, potassium hydroxide (KOH) wet mounts
- Immunology – Quantiferon TB Gold Plus Elisa, PBMC, plasma and serum processing
- RT-PCR – SARS-CoV-2 for COVID-19 (Tembisa only)
- BSL-3 TB lab in Tembisa
- Biorepository

Other protocol-specific testing is contracted to Bio Analytical Research Corporation South Africa (BARC SA) or Clinical Laboratory Services (CLS) in Johannesburg, with a result turnaround time of 48 hours. Includes:
- Haematology – full blood count (FBC) and differential

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“A BSL-3 laboratory is a state-of-the-art containment facility that enables the isolation and manipulation of organisms belonging to risk group three of infectious organisms, i.e. organisms with high individual risk but low community risk, such as drug-resistant TB. They are essential for research and proof-of-concept studies in developing new diagnostics or therapeutics.

“To seek, to find, to share, to care.”
• Chemistry – alanine transaminase (ALT), aspartate aminotransaminase (AST), creatinine
• Serology – Treponema pallidum hemagglutination assay (TPHA), HIV Elisa
• Polymerase Chain Reaction (PCR) – Chlamydia trachomatis, Neisseria gonorrhoea

Shipping of samples: A Laboratory Data Management System (LDMS) is used to manage storage and shipment of samples. Data loggers are used to monitor temperatures of laboratory specimens during transport and shipping. Contracted courier services ship laboratory specimens to specialised local and international laboratories in accordance with local/sponsor Chain of Custody SOPs, and relevant regulations such as International Air Transport Association (IATA) regulations.

f. Data Management
The CRSs have experience with multiple databases, including iDataFax/DataFax, Nucleus, and the MediData RAVE. The Aurum Data Management department has experience designing and using InForm, RedCap, Merge eClinical, and SQL (Structured Query Language). The Aurum Data Management team developed innovative Client Registration and File Tracking (CRaFT) and File Management Tracking systems, which support protocol implementation in the CRSs.

g. Quality Management
CRSs have standard Clinical Quality Management Plans (CQMP) that meet all network/sponsor and protocol requirements. Several quality control tools are used to record and track errors/issues identified. Pharmacy Quality Assurance (QA): Strict systems are in place to maintain data integrity and the quality of research pharmacy services.
Laboratory QA: Aurum research laboratories participate in the following external quality assurance (EQA) programs:

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4South African Health Products Regulatory Authority, previously known as the Medicines Control Council or ‘MCC’
5Division of Acquired Immunodeficiency Syndrome, part of the US National Institutes of Health (NIH)
6Real time RT-PCR is significantly faster than other virus isolation methods and has a lower potential for contamination or errors
One World Accuracy, National Health Laboratory Services, and College of American Pathologists (CAP). Outsourced laboratory services are accredited with South African National Accreditation Services (SANAS) and take part in rigorous laboratory EQA programs: Thistle, CAP, Lancet-BARC, UK National External Quality Assessment Service (UKNEQAS), Quality Assurance Systems International (QASI), and Regional External Quality Assessment Scheme (REQAS).

h. Regulatory Services and Compliance
Aurum has a full, in-house regulatory capacity to ensure participant safety and data quality, and to ensure that studies are conducted in accordance with relevant international and local guidelines. A central Regulatory Manager and Regulatory Officers based at each CRS work closely with study PIs to do regulatory applications and respond promptly to queries to minimise delays in study approvals, and train research staff on audit readiness including document preparation.

The regulatory team has established strong working relationships with local regulatory stakeholders and is experienced in:

- Regulatory submissions for TB vaccines, treatment, and host-directed therapies; HIV vaccines, treatment and prevention; basic science; adolescent research; and cohort studies
- Independent and collaborative submissions with Contract Research Organisations (CROs) and associates
- Compiling study start-up submissions to regulatory authorities
- Compiling and submitting follow-up reports and communications to regulatory authorities for the study duration
- Trial Master File and Investigator Site File design, set-up and maintenance
- Passing audits and monitoring visits by various sponsors and regulatory authorities

Compliance: The Aurum Institute ensures compliance with the following international guidelines: The Belmont Report, The Declaration of Helsinki, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) E6 (R2), Good Clinical Laboratory Practice (GCLP), US Food and Drug Administration (FDA), and the European Medicines Agency (EMA). The CRSs also adhere to the South African guidelines for GCP in the Conduct of Clinical Trials with Human Participants and the South African Department of Health Ethics in Health Research: Principles, Structures, and Processes.

See Annexure 5 for detail on Regulatory Bodies and Aurum Regulatory Processes
i. Advocacy

Aurum is host to the South African Health Technologies Advocacy Coalition (SAHTAC) secretariat. SAHTAC was established after a landscape analysis by the South African Council on Health Research, which identified four key challenges impacting on health research and development (R&D):

1. Governance and commitment to R&D
2. Investment in and incentives for R&D
3. R&D technical skills and capacity
4. Regulatory environment: to adjudicate clinical trials, as well as the registered use of medicines and medical devices, Parliament had replaced the problematic Medicines Control Council with SAHPRA, a new independent public regulator. However, analysis showed that engagement with the national regulator needed to be strengthened, particularly interactions with civil society.

To respond to these issues, SAHTAC aims to create an enabling environment for research, development, and access to life-saving health technologies and innovation. Notable outcomes are to ensure that SAHPRA transparently reports the progress of products as they move through the regulatory process; and promote the capacity of policymakers, regulators, civil society and media among member states of the Southern African Development Community (SADC) to harmonise product regulatory processes across the region.
OUR EXPERTS

Aurum’s clinical research is led by experienced scientists and research managers who have been involved in clinical research for over two decades. They drive the Aurum clinical research agenda, and oversee the development of trial designs and protocol implementation.

Professor Gavin Churchyard, Group Chief Executive Officer and founder of the Aurum Institute, holds an MBBCh, FCP (SA), MMed and PhD. Prof Churchyard is a specialist physician, internationally renowned for his contributions in TB. He is Honorary Professor at the University of Witwatersrand, School of Public Health, and at the London School of Hygiene and Tropical Medicine. Prof Churchyard is a member of the WHO/TDR Disease Reference Group for TB, Leprosy and Buruli Ulcer (which he chaired from 2009 to 2012), and of the WHO Stop TB Research Movement, both of which set global research priorities for TB. At the WHO he also chairs the Task Force for developing policy on new TB drugs, and is member of the TB Strategic Technical Advisory Group, expert committees for TB preventive therapy and TB screening, and the working groups for TB/ HIV, MDR-TB and infection control. Prof Churchyard is co-chair of the NIH HVTN working group on TB vaccines, vice chair of the AIDS Clinical Trials Group Transformative Science Group for TB, and co-chair of a Fogarty Global Infectious Disease training grant for MDR-TB. He is the principal investigator (PI) on a number of TB trials being conducted in South Africa, and is the Principal Investigator of Aurum’s recently awarded DAIDS Clinical Trials Unit (CTU). He has contributed to industry, national and international guidelines for TB and HIV, and has published widely on TB and HIV treatment and prevention.

Professor Vinodh Edward, Regional Chief Operating Officer for Research has been a basic sciences researcher since 2000. He has been involved in clinical research management since 2005. Prof Edward is registered as a professional natural scientist, which allows him to have a broad focus in the biological sciences. He has a good understanding of working with various donors and delivering various projects simultaneously. Prof Edward is passionate about building clinical research capacity in South Africa and strives to achieve efficiencies in all facets of research. He oversees the Clinical Research and Implementation Research Divisions, and is investigator on several clinical trials at Aurum. He is also the Chief Operating Officer of Aurum’s recently awarded DAIDS Clinical Trials Unit (CTU). Prof Edward conceptualised and founded Global Health Innovations, a subsidiary of Aurum, in 2018. GHI provides end-to-end solutions in the public health and research space, and has been instrumental in providing COVID-19 testing and laboratory support since early 2020. He currently serves as GHI’s Chief Executive Officer and is responsible for its strategic direction and business development initiatives. Prof Edward holds a Bachelor of Science degree with majors in Microbiology and Physiology as well as a Doctor of Technology Degree in Biotechnology. He has published in the areas of basic sciences and clinical research.
Ms Tanya Nielson, Managing Director of the Clinical Research Division, is a qualified pharmacist with a Master of Science in Pharmaceutics. With 15 years’ clinical trial experience, she has a very good understanding of the requirements for successful preparation, implementation, and closeout of clinical trials. Her role includes management and oversight of all operational and clinical departments for Aurum’s four clinical research sites, providing cross-site support in trial planning and management, and ensuring that trials are completed according to protocols and standards, within the specified timeframe and budget. As MD, Ms Nielson has overseen implementation of the Sisonke, Ensemble, Ensemble II and Novavax COVID-19 vaccine trials. She currently oversees 39 active research studies and 37 planned studies in the fields of HIV prevention, HIV vaccines, HIV monoclonal antibody, TB treatment, TB vaccines, COVID-19 vaccines and treatment, and COVID-19 monoclonal antibody trials.

Mr Trevor Beattie, Head of Department for Clinical Research, has a Master of Science in Clinical Trials form the London School of Hygiene and Tropical Medicine. He started at Aurum as a Project Coordinator in 2011, and rapidly progressed to Programme Manager of TB Vaccines and Adjunctive Host Directed Therapies before taking up his current role in 2018. He is responsible for the effective delivery of all clinical trials conducted by Aurum, including site development and staff training; study set-up, budgeting, data quality and progress monitoring; sponsor communication and reporting; and supply chain management.

Dr Craig Innes, Clinical Director for the Clinical Research Division, is responsible for overseeing clinical services across multi-site HIV and TB trials in Aurum’s four clinical research sites. Dr Innes has 14 years’ clinical research experience, serving as PI on 15 clinical trials during this period. He was CRS Lead of the Klerksdorp site for five before his appointment as Clinical Director, and is currently Co-Chair of the HVTN 111 study.
OUR EXPERTS

Dr Pearl Selepe, CRS Leader (Klerksdorp), holds an MBChB and has been a clinical research physician since 2007. She was Investigator of Record for the Evidence for Contraceptive Options in HIV Outcomes (ECHO) study, and is responsible for conducting clinical procedures, data collection, protocol-specific eligibility and safety assessments, and ensuring participant safety and timely reporting of adverse events per protocol and regulatory requirements.

Dr William Brumskine, CRS Leader (Rustenburg), is a South African trained medical doctor with a postgraduate diploma in HIV management from the South African College of Family Physicians. He has extensive experience in clinical research management and oversight of multi-site trials, including Investigational New Drug (IND) trials. He has been involved in the conduct of clinical research in HIV and TB for the past nine years, and has been / is currently Principal Investigator on 11 Phase 2 and 3 trials including HIV microbicidal and vaccine trials, TB prevention and treatment studies, and SARS-CoV-2 treatment and vaccine studies. Dr Brumskine has contributed scientifically to Infectious Disease publications since 2016.

Dr Kathy Mngadi, CRS Leader (Tembisa Clinic 4) is an experienced clinical trialist with 18 years’ experience in HIV, TB and recently COVID research trials of all phases. She holds a Master in Palliative Medicine, post-graduate diplomas in HIV Medicine and in Epidemiology, and is completing an MSc in Clinical Trials at the London School of Hygiene and Tropical Medicine. She is the protocol co-chair for the HVTN 107a Phase 2a HIV vaccine study and for the phase 3 Imbokodo study. She is a mentor on the “Retention through Academic Mentoring Program” (RAMP) for disadvantaged medical students interested in doing research in the US. She is a member of the Trial Steering Committee for the PrEPVacc trial, of the Safety Monitoring Committee for the IAVI C100 trial, a review editor on the Frontiers Reproductive Health and STI Journal, and a member of the Oxford Data Access Committee. She sits on the HVTN Scientific Governance Board and Efficacy Working Group, and participated in the WHO Consultation on Planning for the Success of HIV Vaccines in 2018. She serves as Safety Officer for all HVTN trials at the Aurum Institute.
OUR EXPERTS

Dr Modulakgotla Sebe, CRS Leader (Tembisa Clinic 3) has 13 years’ clinical research experience, nine of which he has served as Investigator of Record. He has extensive experience in the management and oversight of multi-site HIV and TB trials. He has worked on research trials of all phases including HIV PrEP, microbicide and vaccine trials; and TB prevention and treatment trials. He has also worked on basic science and Phase 3 influenza studies.

Dr Coert Grobbelaar, CRS Leader (Pretoria), is a clinical research physician and has been principal investigator on clinical trials in a variety of therapeutic areas including vaccines, respiratory, metabolic and infectious diseases. He has experience in early phase inpatient clinical trials. He holds an MBChB and has completed the Global Clinical Scholars in Research programme at Harvard Medical School. He also is a Certified Principal Investigator (CPI) with the Academy of Clinical Research Professionals (ACRP).

"To seek, to find, to share, to care."
C. Our Experience

Experience in complex multi-centre trials: The Klerksdorp, Rustenburg and Tembisa sites have extensive experience in conducting DAIDS network (HVTN and ACTG) and non-network trials and cohort studies. The majority of non-DAIDS funded trials are complex multi-centre trials funded by sponsors outside of Africa.

Recruitment and retention rates in these trials were high. Aurum CRSs have enrolled more than 1,700 participants into HIV vaccine trials and have demonstrated the ability to enrol both high- and low-risk individuals, including participants from key populations (MSM, sex workers, young females, and older males at risk). Aurum contributed 19% of the overall HVTN 702 enrolment and contributed 14% of the 10,629 participants enrolled by the HVTN across all sites between 2014 and 2019.

For HIV prevention studies conducted from 2010 to 2019, HIV incidence rates ranged from 3.6% (MTN003) to 6.1% (HVTN 086) at the Klerksdorp CRS, 1.4% (HVTN 913) to 4.0% (FACTS001) at the Rustenburg CRS and 3.0% (FACTS001) to 5.8% (HVTN107) at the Tembisa CRS. For TB prevention and treatment studies conducted from 2011 to 2018, TB incidence rates among HIV-uninfected adults ranged from 0.5/100py (CORTIS-01) to 1.0/100py (Aeras-GSK TB018) at the Klerksdorp CRS, 0.55/100py (CORTIS 01) to 1/100py (CORTIS HR) at the Rustenburg CRS and 2.5/100py to 2.6/100py at the Tembisa CRS.

Non-vaccine HIV prevention and contraceptive trials: Aurum CRSs have participated in HIV prevention intervention studies with both adult and adolescent populations. The Klerksdorp CRS participated in the VOICE (MTN-003) trial, which tested the safety and effectiveness of the daily use of either an ARV tablet (tenofovir or Truvada) or a vaginal gel (tenofovir gel), as HIV prevention strategies among 5,029 women in Uganda, South Africa, and Zimbabwe. The Rustenburg and Tembisa CRSs participated in FACTS 001, a Phase III trial to assess the safety and effectiveness of 1% tenofovir vaginal gel in the prevention of HIV and HSV infection in young women. The Klerksdorp CRS recently participated in the multicentre ECHO trial (Evidence for Contraceptive and HIV Outcomes). The ECHO Study enrolled 7,829 sexually active, HIV-negative women (ages 16-35), seeking a highly effective contraceptive method across 12 clinical trial sites in Swaziland, Kenya, South Africa, and Zambia.

HIV vaccine trials: Collectively, the three Aurum sites have participated in seven Phase 1 vaccine trials (HVTN 097, HVTN 086, IAVI B003, HVTN 100, HVTN 111, HVTN 107, HVTN 108) and two Phase 2 trials (HVTN 204, HVTN 503). Recent HIV vaccine efficacy trials conducted by the Aurum Institute include three large-scale Phase II/III efficacy trials (HVTN 702, HVTN 703, HVTN 705).

HIV treatment trials: The Tembisa CRS was involved in two Phase IIB trials funded by BMS in 2016 to evaluate the safety and efficacy of an HIV maturation inhibitor drug (BMS- 955176/GSK 3532795) in treatment-naïve and in treatment-experienced HIV infected individuals.
**TB Treatment Trials:** Aurum has participated in several TB treatment trials. The EDCTP-funded Rifaquin trial assessed three regimens of TB treatment for drug-sensitive TB (DS-TB), including moxifloxacin and high-dose rifapentine and found that the 6-month regimen with once-weekly dosing for the last four months was non-inferior to the control, safe and well tolerated. Other TB treatment trials with Aurum participation include Remox, the PANACEA MAMS, and TB Alliance trials (NC-002, NC-005, and NC-006). In addition to clinical trials, Aurum has also conducted epidemiological and strategy trials. TB Fast Track was a cluster-randomized trial to evaluate the effect of a point-of-care TB test-and-treat algorithm on early mortality in people with HIV accessing ART, conducted in 24 primary health centres and involving over 3,000 participants. TB-Sequel is a cohort study among 1,600 TB patients, taking place in Tanzania, The Gambia, Mozambique, and South Africa measuring clinical, microbiological, and socio-economic outcomes. Aurum leads two other projects in the field of TB treatment adherence and M-health applications: the TB Mate Project, evaluating the use of the Wisepill medication box and differentiated care for TB treatment, and a UNITAID-funded project, called Adherence Support Coalition to End TB (ASCENT) project, which will evaluate a variety of treatment adherence technologies for DS-TB and DR-TB.

**TB Prevention Trials:** Aurum has led or participated in landmark studies in the fields of TB preventive therapy and TB vaccines, making the CTU particularly well qualified to contribute to ACTG TB treatment, preventive therapy, vaccine, diagnostic, or strategy trials. Aurum is best known for its work in the field of TB preventive therapy (TPT) in HIV positive populations and other settings. The Thibela TB trial was a cluster-randomized trial of community-wide TPT among 80,000 gold miners in 15 clusters over three provinces in South Africa. Aurum also leads multi-country research trials such as WHIP3TB, which is funded by the Challenge TB project (USAID), evaluating the use of the 3HP regimen for people living with HIV (PLHIV) in 4000 HIV-infected patients in three countries.

“To seek, to find, to share, to care.”
Prof Churchyard is the Chair of the PHOENIx MDR-TB trial, which is evaluating TPT regimens for household contacts of DR-TB patients in 27 sites in 12 countries that will enrol over 3,500 household contacts. Thibela and WHIP3TB laid the foundation for Aurum to lead the Unitaid-funded IMPAACT4TB project, a 12-country study that aims to initiate >400,000 HIV positive people and their household contacts on 3HP, a short-course TPT, with the goal of catalysing the uptake of TPT to reach the global target of 30 million people on TB preventive therapy by 2022. Aurum has also led TB diagnostic, case finding, TB/HIV integration, and strategy trials. Aurum conducted the XTEND trial, a pragmatic cluster randomized trial in 40 primary health clinics across four provinces in South Africa that assessed the effects of replacing smear microscopy with GeneXpert nationally. The MERGE study evaluated the effectiveness of a TB/HIV integration strategy on HIV and TB treatment outcomes. The IBEAT TB study evaluated the mHealth approach to communication of lab results to patients and clinical staff. Other TB case finding projects evaluated digital chest x-rays, new diagnostics, TB contact tracing interventions (Inhibit TB), and TB case finding among special populations such as miners, prisoners and taxi drivers. The XPhactor study evaluated various strategies for TB case finding on HIV positive individuals.

**TB Vaccine Trials:** Aurum has initiated and led TB vaccine trials, including Aurum102/THYB05 H1 in South Africa and Tanzania, and Aeras 402-017 (an Adenovirus type 35-vectored TB vaccine) in HIV-infected adults in South Africa. Aurum participated in the landmark GSK M72/ASO1E TB vaccine trial published in the NEJM and is currently involved in the MESA TB and Aeras-A055 TB Prevention of Recurrence Vaccine trials.

**COVID-19 Trials:** Since March 2020, Aurum’s four Clinical Research Sites have participated in two studies that investigate the natural history, immunology and correlates of COVID-19; and conducted seven SARS-CoV-2 prevention, vaccine, monoclonal antibody and treatment trials. Aurum has enrolled >27,000 participants in COVID-19 trials (including the national Sisonke study), completed >96% of expected visits, and continue to support the national vaccine rollout.
Annexure 1: CRS Staffing Structure

Key: PI = Principle Investigator  SI = Sub-Investigator  RA = Research Assistant  R&R = Recruitment & Retention

Centralised corporate support services

On site, core clinical research services

Managing Director: Clinical Research Division

Operations Director

Programme HOD

Quality HOD

Data HOD

Pharmacy HOD

Lab HOD

Community HOD

Managing Director: Clinical Research Division

Finance

HR

IT

Grants

Regulatory

Clinical Director (PI/SI)

Klerksdorp CRS Leader (PI/SI)

Rustenburg CRS Leader (PI/SI)

Pretoria CRS Leader (PI/SI)

Tembisa CRS Leader (PI/SI)

Multi-site / Multi-study Project Manager

Programme HOD

Quality HOD

Data HOD

Pharmacy HOD

Lab HOD

Community HOD

Programme Manager

Quality Manager

Data Manager

Pharmacy Manager

Lab Manager

Community Manager

Programme Manager

Quality Officer

RA: Data

Pharmacist

RA: R&R

R&R Team Leader

Driver

Lab Tech

Lab Assistant

Site Operations Manager

Site Administrator

Sub-Investigator x 2

Clinic Coordinator

Clinic Administrator

File Administrator

Study Coordinator

Research Nurse x 2

RA: Clinic

On site research support services

Regulatory Manager / Officer

Site Administrator

Sub-Investigator x 2

Clinic Coordinator

Clinic Administrator

File Administrator

Study Coordinator

Research Nurse x 2

RA: Clinic

On site, core clinical research services

“To seek, to find, to share, to care.”
Annexure 2

Annexure 2: CRS Pharmacy and Laboratory Infrastructure and Equipment

KLERKSDORP CRS

Clinic Facilities

Clinic 1: Used for TB treatment studies that enrol infectious TB patients, and prevention of TB recurrence vaccine studies, it has the following infrastructure:
- Reception room with an outside porch and a participant waiting area with UVGI lights as a TB infection control measure for infectious patients, and two counselling rooms
- Clinical consulting rooms x 4 equipped with infusion administration capabilities, and UVGI
- Emergency room (shared with Clinic 2) with a fully equipped emergency trolley containing all basic resuscitation equipment and emergency drugs, which is checked and validated weekly by a registered nurse under the supervision of the Investigator of Record

Clinic 2: Used for TB prevention and TB preventive vaccine studies, it has the following infrastructure:
- Reception, participant waiting area, and counselling room
- Clinical consulting rooms x 3

Clinic 3: Used for active COVID-19 infected studies/trials, it has the following infrastructure
- Reception room
- Donning/doffing room
- Clinical consulting rooms x 2 (one equipped with infusion administration capabilities)
- Counselling rooms x 2

Clinic 4: Used for HIV prevention, HIV and COVID-19 vaccine trials it has the following infrastructure:
- Reception room
- Participant waiting areas x 3 (in the reception, counselling, and clinical areas)
- Counselling rooms x 5
- Clinical consulting rooms x 9
- Supply storage room
- Emergency room

Pharmacy Infrastructure and Equipment

The pharmacy is sub-divided into a combined administration, dispensary, and storage area and a separate preparation area. Shelving is used for the storage of products at ambient room temperature, and study products at controlled room temperature, with space allocated for returned study products, quarantined products, and products for destruction, as well as designated storage for participant files. It is equipped with:
- 1x 2-8°C scientific-grade refrigerator
- 1x commercial 2-8°C refrigerator with six shelves for segregated storage of products
- 2x non-cycling scientific-grade -20°C freezers with chambers for segregated storage at -10°C to -50°C
- 2x non-cycling upright scientific -70°C freezers, with two chambers for storage of products at -60°C to -85°C
• 2x Class IIA biosafety cabinets (BSC) with International Organization for Standardization (ISO) Class 5 air quality, for preparation of sterile products. These are modified with hard ducting so that the air is exhausted externally through a high-efficiency particulate air (HEPA) filter, providing excellent user protection.

**Laboratory Equipment**
- 2x –80°C freezers, 2x -20°C degree freezers, 2x fridges, 3x liquid nitrogen freezers
- 4x Class II biosafety cabinets (BSC), 1x CO2 incubator, 5x refrigerated centrifuges, 2x microscopes, 1x water bath, automated cell counter, washer, reader, shaker, CD4 machine, Haematology analyser
- Clinitek status, 2x label printers, and barcode reader
- Pipette gills, timers, thermometers, laboratory specific furniture and workstations

**RUSTENBURG CRS**

**Adult Clinic**
The reception is used for registration and reimbursement of participants, and is equipped with a biometric co-enrolment prevention system. There are two access-controlled participant waiting areas with a children’s play area. The six counselling rooms are used for individual counselling sessions, interviews, and administration of informed consent. Participant group discussions and Audio Computer-Assisted Self-Interviews (ACASI) are conducted in a dedicated interview room. The 14 clinical consulting rooms are used for patient consultation, examination and biological sample collection, and are fully equipped as a clinical room. A post-vaccination observation area is situated in close proximity to the clinical staff and emergency room, which is equipped with an emergency trolley containing basic resuscitation equipment, emergency drugs, defibrillator, and two electrocardiogram (ECG) machines.

**Adolescent & Youth-friendly Clinic**
The AYFS Clinic is fully equipped to support the specialised needs of adolescents participating in clinical research. The clinic has a physical environment conducive to the provision of adolescent health services, with drugs, supplies, and equipment to provide the essential service package. Adolescents receive information, education, and communication consistent with the essential service package, as well as physical assessments and individualized care aligned with standard service delivery guidelines. Activities available to adolescents include gaming and free Wi-Fi.

It has similar facilities to the Adult Clinic, with a reception area, youth-friendly waiting area, counselling room, interview room, three clinical consulting rooms, and an emergency/resuscitation room.

**Pharmacy Infrastructure and Equipment**
The Rustenburg CRS Pharmacy comprises a waiting area, private counselling area, dispensary with two semi-private dispensing windows, administration area, storage area and a product preparation area. Participant files are stored in the administration area, and study products are stored at controlled room temperature on shelving, with space allocated for returned study products, quarantined products, and products for destruction. It is equipped with:
- 2x 2-8°C commercial refrigerators with six shelves for segregated storage of products
- 2x Non-cycling upright commercial -20°C freezers with chambers for segregated storage at -10°C to -50°C
- 2x Non-cycling upright commercial -70°C freezers, with two chambers for storage at -60°C to -85°C
- 2x Class IIB2 BSC with ISO Class 5 air quality for the preparation of sterile products
Laboratory Infrastructure and Equipment

The on-site access-controlled laboratory consists of a receiving area for receipt and logging of samples, sample testing areas, separate areas for PBMC and plasma/serum processing, and storage and administration areas.

- 2x 2-8°C fridges, 2x -20°C freezers, 2x -80°C freezers, 3x liquid nitrogen freezers
- 3x Class II BSC, 6x centrifuges, 1x CO2 incubator, 2x microscopes
- 1x Becton Dickinson Fluorescence-Activated Cell Sorting (FACS) counter for cluster of differentiation (CD4/CD8) counts
- 1x Digisystem Rotator DSR 2800V and 1x Finevortex mixer for PCR
- 6x analysers including one Beckman Coulter DXH 500 for full blood counts
- 1x Cepheid GeneXpert fourth-generation for Neisseria gonorrhoea, Chlamydia trachomatis, viral load testing
- 1x Biotek ELX 50 and 1x Biotek ELX 800 washer
- Pipette gills, timers, thermometers, laboratory specific furniture and workstations, printers, desktop computers and laptops

TEMBISA CRS

Clinic Infrastructure and Equipment

Studies that enroll infectious TB patients for treatment are conducted in Clinic 1. TB prevention studies are conducted in Clinic 2, and HIV prevention and treatment studies take place in Clinics 3 and 4. Participants with active TB are dispensed study product in-clinic and do not access the CRS pharmacy. All four clinics have the following facilities:

- **Participant waiting areas**: Each clinic has a waiting area. Clinics 2 and 4 have four and three Counselling Rooms respectively for individual participant counselling and interviews.
- **Clinical consulting rooms**: Clinics 1, 2, and 4 have three rooms each, and Clinic 3 has seven rooms, which are fully equipped and utilized for patient consultation, examination, and biological sample collection, as well as vaccine administration. Clinic 3 has one room adapted as a designated infusion room.
- **Emergency rooms**: Each clinic has an emergency room equipped with an emergency trolley with the necessary emergency equipment and drugs, and a defibrillator.

In addition, Clinic 1 has specialised clinical assessment facilities for spirometry and six-minute walk testing. The clinics are equipped as follows:

<table>
<thead>
<tr>
<th>Admin Offices</th>
<th>Biometric Co-Enrolment Prevention System (SAMRC)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consulting Rooms</strong></td>
<td>Examination beds and steps, drip stands, medical trolleys, wall mounted ophthalmoscopes /otoscopes, vital signs devices, thermoscans height meters, digital weight scales, examination lamps, eyewash stations, washbasins, and an x-ray light</td>
</tr>
<tr>
<td><strong>Infusion room (Clinic 3)</strong></td>
<td>Reclining chair, drip stands, electronic infusion pumps, a large medical trolley, an emergency bag (Infusion room-Clinic Three)</td>
</tr>
<tr>
<td><strong>Emergency rooms</strong></td>
<td>Fully equipped with medical examination bed, medical trolley, emergency trolley with emergency equipment, necessary emergency drugs, and a defibrillator</td>
</tr>
<tr>
<td><strong>Spirometry room (Clinic 1)</strong></td>
<td>Spirometer with uploaded Easy-on-PC software, which provides spirometry data and spirographs. Specialized equipment for NIOX Fractional Exhaled Nitric Oxide (FeNO) to assess airway inflammation and perform Diffusion Capacity of the Lung for Carbon Monoxide (DLCO) testing</td>
</tr>
<tr>
<td><strong>Six-minute walk testing</strong></td>
<td>A 12m line is printed on the floor at 1m increments to measure the distance an individual is able to walk over six minutes on a hard, flat surface. A sub-maximal exercise test, it is used to assess aerobic capacity, endurance, and general physiological well-being.</td>
</tr>
</tbody>
</table>
Pharmacy Equipment
The pharmacy includes a waiting area, private counselling areas, a dispensary with four dispensing counters and semi-private counselling areas, preparation area, and a bulk storage area with refrigeration and freezing equipment and shelving for storage of products at room temperature. Participant files are stored in lockable mobile bulk high-density steel fire-resistant filing cupboards in the filing area. It is equipped with:
- 2x 2-8°C scientific-grade refrigerators with six shelves for segregated storage of products
- 2x Non-cycling upright scientific-grade -20°C freezers with chambers for segregated storage at -10°C to -50°C
- 2x Non-cycling upright scientific-grade -70°C freezers, with two chambers for storage at -60°C to -85°C
- 2x Class IIA BSC with ISO Class 5 air quality for the preparation of sterile products

<table>
<thead>
<tr>
<th>Receiving area</th>
<th>LABWARE management system for logging samples and capturing results</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSL-3 Main Laboratory</td>
<td>Beckman Centrifuge, fridges, ultralow freezer, BACTEC Mycobacterial Growth Indicator Tube (MGIT) 320, orbital shaker, CO2 incubator, laboratory autoclave, mini centrifuge, laminar flow safety hoods, vortex mixer, water cooler</td>
</tr>
<tr>
<td>Bacteriology Lab</td>
<td>Heating plate, incubator, shaking incubator, water bath, biosafety cabinet, Thermo spectrophotometer, and vortex mixer</td>
</tr>
<tr>
<td>TB Lab</td>
<td>BACTEC MGIT 960, bar fridge, BRL Xpert 002, GeneXpert</td>
</tr>
<tr>
<td>Microscopy room</td>
<td>CARL ZEISS Primo Star microscope and fluorescent microscope</td>
</tr>
<tr>
<td>Bioluminescent Lab</td>
<td>BM-Thermostat Microplate incubator shaker, microplate counter, digital sonifier, heat sealer, suction pump, filter mate harvesters, chemical spill kit</td>
</tr>
<tr>
<td>Serology Lab</td>
<td>HERMLE Z3000 micro-centrifuge, Labcon distilled water, fridges, ice-maker, CARL ZEISS light microscope, BioTek ELISA Microplate reader and plate washer.</td>
</tr>
<tr>
<td>PCR room</td>
<td>Balance scale, chemical storage cabinets, E-gel imager, fluorometer, magnetic stirrer, mini centrifuge, thermos cycler</td>
</tr>
<tr>
<td>Cytometry room</td>
<td>Bio-rad Powerpac, centrifuge, Labcon magnetic stirrer, micro centaur, microwave, fridge</td>
</tr>
<tr>
<td>Short-term storage</td>
<td>Biosafety cabinets (BSC), printer, BRL BSC 003 and 005, centrifuges, Clintek status, label meter, HERAEUS MEGAFIGE 16R centrifuge, medical scales, microscope, muse cell counter, oxygen meter, incubator, lab freezer, ultralow temperature freezer, -30° freezer, temperature meter, vortex mixer</td>
</tr>
<tr>
<td>Repository</td>
<td>CBS BRL-LN2-002, Omniflex temperature monitor, BRL-FRE-001, 003 and 004, TEM-LE-04, and Taylor-Wharton 24 K series Cryogenic systems.</td>
</tr>
</tbody>
</table>
Annexure 3:

Key Demographic Features of CRS Study Populations

**KLERKSDORP CRS**
The Klerksdorp CRS is located in a peri-urban area within the City of Matlosana Local Municipality, in the Dr Kenneth Kaunda District, North West Province (NWP) of South Africa, 99 miles southwest of Johannesburg.

**Community Socio-Demographic Profile:** In 2019, the population of Matlosana was 456,453 (92% urbanized, 8% rural). In 2016, the population of NWP was 82.6% black African, 3.2% mixed-race, 0.7% Indian/Asians, and 13.5% whites, with ~63% of the population aged between 15-59 years. 89.1% of households live in formal dwellings, and 68.7% of individuals >20 years of age completed secondary education. Setswana is spoken by >70% of the population.

**HIV Epidemiology:** In 2017, a household survey estimated the adult (15-49 years) prevalence of HIV in the NWP as 22.7%. Similarly, the Thembisa model showed a prevalence of 20.0% and incidence of 1.2%. The HIV prevalence amongst antenatal women in the Dr Kenneth Kaunda Health District was 33.9%. HIV incidence among high-risk participants in HIV prevention trials ranges from 3.6 to 6.1 per 100 person-years (PYs).

**TB Epidemiology:** According to the District Health Barometer report TB incidence in the NWP and Dr Kenneth Kaunda Health District in 2016 was ~429/100,000 and ~578/100,000 respectively. It reported a TB treatment initiation rate of 80.6% in 2017/2018, 68.0% of TB patients were HIV co-infected, and 6.6% were rifampicin-resistant.

**RUSTENBURG CRS**
The Rustenburg CRS is located in the Rustenburg Local Municipality of the Bojanala Platinum District, NWP, 64 miles from Johannesburg.

**Community Socio-Demographic Profile:** The population of Rustenburg is 632,000 (45.8% female), consisting of 89.7% black Africans, 8.5% whites, 0.9% mixed-race, and 0.9% Indians/Asians. There are > 3,000 FSW and >8,000 MSM in Bojanala. 68.2% of households live in formal dwellings, and 74.7% of the population is >20 years and has completed secondary education. Setswana is spoken by >70% of the population.

**HIV Epidemiology:** In 2017, a household survey estimated the adult (15-49 years) prevalence of HIV in the NWP as 22.7%. Similarly, the Thembisa Model estimated a prevalence of 20.0% and an incidence of 1.2%. HIV prevalence amongst antenatal women in the Bojanala Platinum District was
28.6%. In an observational cohort study of high-risk men, the HIV-incidence was 1.9 per 100 person-years (PYs).

TB Epidemiology: According to the Department of Health statistics, there were approximately 442/100,000 reported TB cases in NWP in 2017, with approximately ~305/100,000 in the Bojanala district. In 2017, 6.4% of TB patients were rifampicin-resistant, and 85.3% of TB patients who were HIV co-infected were on ART.

**TEMBISA CRS**

The Tembisa CRS is ideally situated on the grounds of the Tembisa Tertiary Hospital in the urban township of Tembisa in the City of Ekurhuleni Metropolitan Municipality, Gauteng Province, 30 miles northeast of Johannesburg.

**Community Socio-Demographic Profile:** The population of the City of Ekurhuleni is 3,379,104, consisting of 81.7% black Africans, 2.5% mixed-race, 2.0% Indians/Asians and 13.7% whites. Approximately 66% of the population is aged 15-64 years. 80.4% of households live in formal dwellings, and 77.7% of the individuals aged 20 years and older have completed secondary education. IsiZulu is the predominant language spoken by 23% of the population in Gauteng.

**HIV Epidemiology:** In 2017, a household survey estimated the HIV prevalence among adults 15-49 years in Gauteng Province as 17.6%. Similarly, the Thembisa model estimated a prevalence of 18.0% and an incidence of 0.92%. HIV prevalence amongst antenatal women in the City of Ekurhuleni was 32.2%.

**TB Epidemiology:** According to the Department of Health statistics, TB incidence in Gauteng and Ekurhuleni Health district in 2017 was approximately 288/100,000 and ~268/100 000, respectively. In 2017, 6.1% of TB patients were rifampicin-resistant, and 86.1% of TB patients with HIV co-infection were on ART.
Annexure 4: Project Experience in Managing Investigational Products

Aurum has the following experience in managing investigational products for clinical trials

1. Phase II double-blind, randomized, placebo-controlled study to evaluate safety and immunogenicity of H1/Ic31® in HIV-infected adults with CD4+ lymphocyte counts greater than 350 cells/mm³

Aurum coordinated the receipt, import, cold chain and distribution of 96 vaccine doses of the H1/Ic31® adjuvant TB subunit vaccine for 48 subjects at the Aurum Tembisa Clinical Research Site (CRS), South Africa and the Ifakara Health Institute, Tanzania.

2. Phase II, randomized, open-label trial to evaluate safety, preliminary efficacy, and biomarker response of host directed therapies added to Rifabutin-modified standard antimicrobial therapy in adult patients with drug-sensitive, smear-positive pulmonary TB (TB HDT)

Aurum procured and repackaged study arm-specific Rifabutin-substituted standard TB therapy with adjunctive TB Host Directed Therapies into daily doses in polytops using a GMP certified drug distribution and repackaging facility. Drug procurement, packaging and distribution were complicated by:

- Trial design, multi-arm multi centre, where 200 adult HIV negative DS-TB positive with moderate to far advanced TB disease graded by radiographic assessment were enrolled across three South African research sites, across the following 5 arms stratified by site and extent of disease:
  - Rifabutin substituted standard TB therapy alone (control)
  - Rifabutin substituted standard TB therapy plus AMG-634, formerly CC11050 200mg BID
  - Rifabutin substituted standard TB therapy plus everolimus 0,5mg QD
  - Rifabutin substituted standard TB therapy plus auranofin 3mg QD for 1 week, then 6mg QD
  - Rifabutin substituted standard TB therapy plus Vitamin D2, a total of 3 doses: 5mg initially (day 0), then 2.5mg Q month for 2 doses, days 28 and 56

- Lack of availability of registered drug stocks with favourable shelf-life / early expiring stock
- Ceased production of Auranofin by Astellas, Italy mid-trial whilst sourcing new Sebela product at triple the cost. This forced the Aurum drug management group to issue the instruction to repackage later visit doses into earlier doses for newly enrolled participants and to temporarily halt enrolment into the Auranofin arm until new stocks arrived. No Auranofin doses were missed during this time.
3. Phase I/II trial to evaluate safety, tolerability, and drug-drug interactions of short-course treatment of latent TB infection with high-dose rifapentine and isoniazid vs. standard isoniazid preventative therapy among HIV-infected patients taking dolutegravir-based antiretroviral treatment (DolPHIn). Twelve doses of once weekly isoniazid and rifapentine were dispensed to 75 participants across 3 arms.

4. Phase IIb, open-label, randomized controlled dose multi-centre trial to evaluate the safety, tolerability, pharmacokinetics and exposure response relationship of different doses of Sutezolid in combination with Bedaquiline, Delamanid and Moxifloxacin in adult subjects with newly diagnosed, uncomplicated, smear-positive, drug-sensitive pulmonary TB. The Sudocu TB treatment trial started in June 2021, will enrol 75 participants in South Africa and Tanzania, and requires the procurement, labelling and distribution of moxifloxacin, bedaquiline and sutezolid.

5. Pan-TB HM and DRTB-HDT: funded by the EDCTP and the European Commission Horizon 2020 call respectively, these two large Aurum investigator-initiated trials are commencing in 2021. 
   • Pan-TB HM: Drugs will be procured (Delaminid, Bedaquiline, and N-acetylcysteine) and manufactured (Sutezolid), repackaged at a GMP facility into daily dose arm specific dosages and distributed to Wits CHRU, Tembisa CRS and the Aurum Mozambique CRS.
   • DRTB-HDT project will source standard of care Rif-R TB treatment from country specific local TB programmes, and adjunctive HDTs, metformin and AMG-634 will be repackaged at a GMP facility into daily dose arm specific dosages. Drugs destined for EU sites in Georgia, Moldova, Romania, Belgium and Germany will be shipped by Pharma Logistics to a central drug distribution and storage centre in Hungary. Similarly, Aurum sites in Southern Africa and Mozambique will have drugs shipped centrally from Pharma Logistics’ centre in Centurion, South Africa.
Annexure 5: Regulatory Bodies and Aurum
Regulatory Processes

REGULATORY BODIES

New study protocols are submitted to Independent Ethics Committees (IECs) for approval. In addition, each protocol is submitted for review and approval to the National Drug Regulatory Authority (NDRA) and other national and local regulatory authorities before study implementation.

National Drug Regulatory Authorities (NDRA) such as the South African Health Products Regulatory Authority (SAHPRA) and Tanzania Food and Drugs Authority (TFDA) are responsible for reviewing pre-clinical data and study Investigator Brochures (IBs) prior to approval as well as evaluating safety and efficacy data from clinical trials, inspecting facilities, controlling drug promotion, and monitoring adverse reactions. Investigators are required to obtain all the necessary NDRA approvals prior to study implementation.

- Initial submission: Clinical Trial Application Form, protocol, Informed Consent Forms (ICFs), IBs, Package Inserts, sponsor indemnity, study budgets, and insurance. Study PIs and key staff are required to submit CVs, GCP certificates, proof of professional registration, and declarations/workloads (if required). The NDRA must be informed of a study’s initial IEC approval. SAHPRA reviews and approves all study PIs and research doctors and requires notification of all pharmacists working on a study.

- Subsequent submissions: Progress reports, protocol amendments, protocol deviation reports, adverse event (AE) reporting, updated IBs/Package Inserts, and safety reports.

Independent Ethics Committees (IECs) safeguard the dignity, rights, safety, and well-being of research participants. They review, approve, and comments on clinical trial protocols, the suitability of study PIs, facilities, and methods and procedures used to obtain informed consent. All ongoing protocols are submitted annually to Aurum’s local IEC, the University of the Witwatersrand Human Research Ethics Committee (WITS-HREC), for review and recertification.

- Initial submission: Cover letter, protocol, ICFs, questionnaires, IBs/Package Inserts, study budgets, and insurance. The study and key staff submit CVs, declarations, GCP certificates, and proof of professional registration. The IEC must be informed of the study’s initial NDRA approval.

- Subsequent submissions: Progress reports, annual recertification of all studies, protocol amendments, protocol deviations, critical events, AE reporting (including serious AEs), and safety reports. The IEC may also review and approve study PIs, new research doctors, CRS Leaders (CRSL), and pharmacists.
Other Requirements: Depending on the type of research and in-country guidelines, further approvals may be required, for instance:

- **National Health Regulatory Bodies:** are responsible for improving the health status and healthcare for the people of their country. They provide a regulatory framework for health research and integrate science and technology into the national development process. The South African National Department of Health (NDOH) needs to be informed of all health research and clinical trials that are being conducted in the country, and their approval is required prior to commencing a study, obtained through the National Health Research Database (NHRD).

- **Provincial and District/Metropolitan Health Approvals:** In South Africa, approval from the Provincial Department of Health (PDOH) is required if studies are conducted or participants recruited at public health facilities, and is obtained via the NHRD. District/Metro approval is required if > 4 facilities in a particular District/Metro are used.

- **Research Involving Genetically Modified Organisms (GMOs):** Institutional Biosafety Committees (IBCs) review research involving recombinant and synthetic nucleic acid molecules. When the investigational product (IP) is a GMO, the trial must comply with national legislative guidelines regarding the contained use of GMOs and/or deliberate release of GMOs in the environment and must seek approval from a National Biosafety Authority such as the South African Department of Agriculture, Forestry and Fisheries (DAFF) and/or IBC.

- **Biobanks:** In South Africa, all new repositories require approval from an IEC before storing samples. The Tembisa Biomedical Research Laboratory (BRL) has a biobanking facility accredited with the WITS Biobanks Ethics Committee (WITS-BEC). Outsourced laboratories [i.e. Clinical Laboratory Service (CLS) and Bio Analytical Research Corporation (BARC)] have accredited biobanking facilities approved by the WITS-BEC.

- **Other entities, such as the WHO Food and Drugs Authority**

**Clinical Trial Registration:** Sponsors and in-country guidelines require online registration of trials, so that information is easily accessible. PIs ensure that all clinical trials are registered in one or more of the following:

- **South African National Clinical Trial Register (SANCTR):** Clinical trial registration on SANCTR is required by law, using the National Health Research Ethics Council (NHREC) online ethics application system. Once SAHPRA and IEC approval are received, SANCTR is updated, and the NDOH issues a National Register Number.

- **Pan African Clinical Trials Registry (PACTR):** PACTR is an open-access register of clinical trials conducted in Africa; it feeds into the World Health Organization International Clinical Trials Registry.

- **ClinicalTrials.gov:** All clinical investigations of US-FDA regulated drugs or biological products (except phase I studies) must be registered on this database.

While the timeline for regulatory approvals is highly dependent on the complexity of the protocol (e.g. if requiring GMO approval), given Aurum’s long-standing institutional relationships with in-country regulatory administrators, average timelines for approval (tabulated) are highly competitive with international norms.

<table>
<thead>
<tr>
<th>Regulatory Authorities</th>
<th>Approval timelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAHPRA</td>
<td>2-4 months</td>
</tr>
<tr>
<td>WITS-HREC</td>
<td>1-2 months</td>
</tr>
<tr>
<td>NDOH and PDOH</td>
<td>1-2 months</td>
</tr>
<tr>
<td>DAFF and WITS-IBC (GMO approval)</td>
<td>6 months</td>
</tr>
</tbody>
</table>
The regulatory department oversees and tracks all regulatory submissions and approvals. The study PI works with the regulatory team to obtain annual recertification from IECs, and approval of protocol amendments and updated study documents. Relevant authorities are informed in a timely fashion of critical events, social harms, protocol violations/deviations, adverse events, Data and Safety Monitoring Board (DSMB) reports, and safety reports.

The regulatory submission and approval process for a new protocol is as follows:

1. A new clinical trial is registered on the NHREC website.
2. Applications are submitted in parallel to SAHPRA and the WITS-HREC. Once submitted, an application is made on the NHRD website to seek PDoH approval. If the IP is a GMO, an application is also submitted to DAFF.
3. WITS-HREC and SAHPRA approvals are sent to the SANCTR and NHRD websites for NDOH and PDoH approvals. If the IP is a GMO, HREC and SAHPRA approvals are submitted together with an application to the WITS IBC. DAFF authorization is dependent on SAHPRA approval.
4. The Regulatory team inform the study PI and CRSL once all initial regulatory approvals are obtained.
5. Once all the necessary approvals are in place, the CRS implements the protocol.
**Regulatory Compliance:** The Aurum team has developed an innovative Central Projects Database that maintains, tracks and coordinates all regulatory activities for all studies conducted at the CRSs. The database also tracks and pro-actively alerts staff about annual re-certifications of studies and progress reports to ensure timely submissions to regulatory authorities. The Aurum Institute conducts studies in accordance with the study protocol and study and non-study specific Standard Operating Procedures (SOPs). As described below, the Aurum Institute also ensure compliance with all relevant national and local guidelines and requirements.

- **SA/ICH GCP:** The regulatory and training team ensures that relevant staff receives face-to-face GCP training by an accredited service provider and refresher training every three years. Training certificates for key staff are submitted with CVs and supporting documents to the applicable regulatory authorities. Electronic copies of certificates are systematically filed, and hard copies are maintained in the essential document binders.

- **Changes from National and Local Regulatory Authorities:** The IEC informs the regulatory team of any changes to regulatory guidelines and local policies. National regulatory authorities convene annual meetings to inform stakeholders of new guidelines and proposed future updates. Regulatory team members who are part of the South African Clinical Research Association (SACRA) attend quarterly SACRA meetings and receive email alerts regarding updates/changes to local or national regulations.

- **Study start up requirements:** Once a study is awarded, the CRS will work through a checklist of activation requirements. Activation and project management tools are combined into a spider diagram and a dashboard report that is continuously updated. The study PI is responsible for ensuring that regulatory approvals have been obtained, and the staff has the necessary qualifications and training. The CRS will conduct a mock run of visits to ensure that staff is familiar with the processes and to identify potential challenges. Source documents may be revised and procedures updated if required. Once a site has been activated, the CRS team needs to ensure that protocol deviations, violations, or critical events are reported to the sponsor and regulatory authorities promptly. Any amendments to study documents are submitted to the regulatory authorities; once approvals are received, training and implementation are facilitated.
Regulatory Agency Inspection: Internal quality processes ensure that the CRSs are inspection-ready at all times. The CRS and quality team review all study-related activities and conduct periodic internal process reviews to ensure that procedures are being conducted as per SOPs and protocol-specific guidelines. External monitoring contractors perform quarterly reviews of study documentation and data. The CRS Leader and Coordinator ensure timely resolution of all findings and queries. The study PI and CRS Leader are alerted to challenges so that processes/procedures may be evaluated, and training can be provided across CRSs. Key findings are also shared across CRSs so that processes can be improved.

The CRSs have undergone and passed several rigorous audits and monitoring visits by various sponsors and auditors, as tabulated below. All findings from inspections were adequately addressed and feedback provided to the relevant regulatory agency. All findings were shared with CRS staff, and retraining was conducted where required. Systems were developed to improve processes at the CRS.

In addition to the audits listed below, CRSs have also undergone various Laboratory GCLP audits, performing adequately with no major findings.

### Key to Clinical Trial Sites (CRS):

- KLD = Klerksdorp
- RTB = Rustenburg
- TMB = Tembisa
- PTA = Pretoria

<table>
<thead>
<tr>
<th>Conducted by</th>
<th>Studies reviewed</th>
<th>CRS</th>
<th>Year</th>
<th>Inspection type and key processes / documentation checked</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCC (now SAHPRA)</td>
<td>FACTS 001</td>
<td>RTB</td>
<td>2013</td>
<td><strong>GCP audit:</strong> Essential documents, participant binders, Informed Consent Forms (ICF), training documents, SOPs, pharmacy, lab</td>
<td>3 critical findings** Minor 6</td>
</tr>
<tr>
<td>MCC (now SAHPRA)</td>
<td>NC006*</td>
<td>RTB</td>
<td>2014</td>
<td><strong>GCP audit:</strong> Essential documents, participant binders, ICFs, training documents, SOPs, pharmacy</td>
<td>No critical findings Major 1 Minor 5</td>
</tr>
<tr>
<td>MCC (now SAHPRA)</td>
<td>NC006*</td>
<td>TMB</td>
<td>2015</td>
<td><strong>GCP audit:</strong> Essential documents, participant binders, ICFs, training documents, SOPs, pharmacy</td>
<td>No critical or major findings</td>
</tr>
<tr>
<td>SAHPRA</td>
<td>TB HDT</td>
<td>TMB</td>
<td>2017</td>
<td><strong>GCP audit:</strong> Facilities, staff interviews, essential documents, participant binders, ICFs, training documents, SOPs, pharmacy</td>
<td>Only minor findings that were adequately addressed</td>
</tr>
<tr>
<td>DAIDS</td>
<td>HVTN 702 HVTN 703/ HPTN 081</td>
<td>RTB</td>
<td>2018</td>
<td><strong>GCP audit:</strong> Essential documents, participant binders, ICFs, training documents, SOPs, pharmacy, lab</td>
<td>No critical findings Major 9*** Minor 19</td>
</tr>
<tr>
<td>SAHPRA</td>
<td>Ensemble</td>
<td>RTB</td>
<td>2021</td>
<td><strong>GCP audit:</strong> Essential documents, participant binders, ICFs, training documents, SOPs, pharmacy and lab</td>
<td>Major findings 2****</td>
</tr>
<tr>
<td>SAHPRA</td>
<td>Ensemble II PTA</td>
<td>2021</td>
<td>Unannounced virtual GCP inspection: Protocol, SOPs, other regulatory requirements relating to participants</td>
<td>No notable findings</td>
<td></td>
</tr>
</tbody>
</table>

* Two deaths were experienced in the study (both at the Aurum sites), which led to the audits.

** The three critical findings related to guidance received from the protocol team, and a lack of coordination between the team and site. The CRS and protocol team were adequately able to resolve all findings with the regulatory agency.

*** Major findings: 1. Documentation of training. 2. Checks of emergency drugs/equipment not consistently performed at the frequency described in the SOP. 3. Discrepant serial numbers on the CTMS probe and calibration certificates. 4. Non-adherence to the Quality Management Plan. 5. One enrolled participant did not meet inclusion criteria. 6. Inadequate documentation of protocol deviations. 7. Procedures/documentation related to infusion administration not in accordance with the study SSP manual. 8. Inadequately administered informed consent process. 9. Misplaced locator and inadequate/improper corrections to case report forms. The CRS worked on comprehensive corrective and preventative action plans and implemented quality improvement processes to prevent the recurrence. All findings were satisfactorily resolved.

**** Major findings related to the ICF process and delayed follow up of external results. These were due to the PI being booked off for an extended period for COVID-19. The CRS worked on comprehensive corrective and preventative action plans and implemented quality improvement processes to prevent the recurrence. All findings were satisfactorily resolved.
# Annexure 6: Aurum Clinical Trial Projects (2012 - present)

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<tr>
<th>Study/Trial (Phase)</th>
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<th>Study Description</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV Vaccine Trials</strong></td>
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</tr>
<tr>
<td>IA VI B003 (I)</td>
<td>IAVI</td>
<td>2011-</td>
<td>A Phase 1 placebo controlled, double blind, randomised trial to evaluate the safety and immunogenicity of Ad26-ENVA and Ad35-ENV HIV vaccines in healthy HIV-uninfected adult volunteers</td>
<td>KLD</td>
<td>27</td>
<td>100%</td>
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<tr>
<td></td>
<td></td>
<td>2012-</td>
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<tr>
<td></td>
<td></td>
<td>2012-</td>
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<td></td>
</tr>
<tr>
<td>HVTN 086 (I)</td>
<td>NIH/HVTN</td>
<td>2012-</td>
<td>A phase 1 placebo-controlled clinical trial to evaluate the safety and immunogenicity of SAAVI DNA-C2, SAAVI MVA-C and Novartis subtype C gp140 with MF59 adjuvant in various vaccination schedules in HIV-uninfected healthy vaccinia-naïve adult participants in South Africa</td>
<td>KLD</td>
<td>62</td>
<td>84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2013-</td>
<td></td>
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<tr>
<td>HVTN 097 (Ib)</td>
<td>NIH/HVTN</td>
<td>2013-</td>
<td>A Phase1B Randomized Double Blind Placebo Controlled Clinical Trial to Evaluate the Safety and Immunogenicity of the Vaccine Regimen ALVAC-HIV (Vcp1521) followed by AIDSVAX® B/E in Healthy, HIV-1 Uninfected Adult Participants in South Africa</td>
<td>KLD</td>
<td>33</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2015-</td>
<td>A Phase 1-2 randomized, double-blind, placebo-controlled clinical trial of clade C ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59® in HIV-uninfected adults at low risk of HIV infection</td>
<td>KLD</td>
<td>36</td>
<td>99%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2016-</td>
<td>A phase 1 clinical trial to evaluate the safety and immunogenicity of HIV clade C DNA and of MF59 - adjuvanted clade C Env protein, in healthy, HIV-uninfected adult participants</td>
<td>KLD</td>
<td>43</td>
<td>up to 100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2017-</td>
<td>A Phase 1/2a clinical trial to evaluate the safety and immunogenicity of HIV clade C DNA, and of MF59®- or AS01B-adjuvanted clade C Env protein, in various combinations, in healthy, HIV-uninfected adult participants</td>
<td>KLD</td>
<td>32</td>
<td>up to 100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2017-</td>
<td>A Phase 1/2a double-blind, randomized clinical trial to characterize the safety and immunogenicity of clade C ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59® and alum adjuvant in healthy, HIV-uninfected adult participants</td>
<td>TMB</td>
<td>20</td>
<td>68%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2017-</td>
<td>A pivotal phase 2b/3 multi-site, randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59 in preventing HIV-1 infection in adults in South Africa</td>
<td>KLD, RTB, TMB</td>
<td>1001</td>
<td>up to 90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2018-</td>
<td>A Phase 2b Study to Evaluate the Safety and Efficacy of VRC01 Broadly Neutralizing Monoclonal Antibody in Reducing Acquisition of HIV-1 Infection in Women in Sub-Saharan Africa</td>
<td>KLD, RTB, TMB</td>
<td>70</td>
<td>up to 97%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2019-</td>
<td>A multicenter, randomized, double-blind, placebo-controlled phase 2b efficacy study of a heterologous prime/boost vaccine regimen of Ad26.Mos4.HIV and aluminum phosphate-adjuvanted Clade C gp140 in preventing HIV-1 infection in adult women in Sub-Saharan Africa</td>
<td>KLD, RTB, TMB, ZEHRP Ndola</td>
<td>283</td>
<td>up to 98%</td>
</tr>
<tr>
<td><strong>HIV Prevention Trials</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MTN 003 (Ib)</td>
<td>NIH/MTN</td>
<td>2010-</td>
<td>Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate Tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women</td>
<td>KLD</td>
<td>263</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2013-</td>
<td></td>
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<td></td>
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<tr>
<td>MTN 015</td>
<td>NIH/MTN</td>
<td>2010-</td>
<td>Observational Cohort Study of Women following HIV-1 Seroconversion in Microbicide Trials</td>
<td>KLD</td>
<td>12</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2013-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTN 016</td>
<td>NIH/MTN</td>
<td>2010-</td>
<td>HIV Prevention Agent Pregnancy Exposure Registry: EMBRACE Study</td>
<td>KLD</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2013-</td>
<td></td>
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</tbody>
</table>
### Annexure 6: Aurum Clinical Trial Projects (2012 - present)

<table>
<thead>
<tr>
<th>Study/Trial (Phase)</th>
<th>Sponsor Network</th>
<th>Duration</th>
<th>Study Description</th>
<th>CRS</th>
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</tr>
</thead>
<tbody>
<tr>
<td>FACTS 001 (III)</td>
<td>CONRAD/FACTS</td>
<td>2011-2014</td>
<td>A Phase III, Multi-Centre, Randomised Controlled Trial to Assess the Safety and Effectiveness of the Vaginal Microbicide 1% Tenofovir Gel in the Prevention of Human Immunodeficiency Virus Type 1 Infection in Young Women, and to Examine Effects of the Microbicide on the Incidence of Herpes Simplex Virus Type 2 Infection</td>
<td>RTB, TMB</td>
<td>619</td>
<td>up to 85%</td>
</tr>
<tr>
<td>FACTS 001B</td>
<td>CONRAD/FACTS</td>
<td>2015-2016</td>
<td>Observational Cohort SubStudy of FACTS 001 Participants Post-Withdrawal from Placebo or Tenofovir 1% Vaginal Gel Use</td>
<td>RTB, TMB</td>
<td>256</td>
<td>n/a</td>
</tr>
<tr>
<td>ECHO</td>
<td>FHI360</td>
<td>2016-2018</td>
<td>A Multi Center, Open-Label, Randomised Clinical Trial Comparing Incidence of HIV and Pregnancy in Women using Progestin-Only Injectable, Levonorgestrel Implants, and Copper IUDs</td>
<td>KLD</td>
<td>555</td>
<td>93%</td>
</tr>
</tbody>
</table>

### HIV Treatment Trials

<table>
<thead>
<tr>
<th>Study/Trial (Phase)</th>
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<th>Study Description</th>
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</tr>
</thead>
<tbody>
<tr>
<td>BMS 048 (IIb)</td>
<td>BMS</td>
<td>2015-2016</td>
<td>A Phase 2b Randomized, Active-Controlled, Staged, Open-Label Trial to Investigate Safety and Efficacy of BMS-955176/GSK3532795 in Combination With Dolutegravir and Atazanavir (With or Without Ritonavir) in Treatment-Experienced HIV-1 Infected Adults</td>
<td>TMB</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

### TB Prevention Trials

<table>
<thead>
<tr>
<th>Study/Trial (Phase)</th>
<th>Sponsor Network</th>
<th>Duration</th>
<th>Study Description</th>
<th>CRS</th>
<th>Enrolled</th>
<th>Retained</th>
</tr>
</thead>
<tbody>
<tr>
<td>CORTIS 01</td>
<td>UCT</td>
<td>2016-current</td>
<td>A Randomized, Partially-blinded, Clinical Trial of Isoniazid and Rifapentine (3HP) Therapy to Prevent Pulmonary Tuberculosis in High-risk Individuals Identified by a Transcriptomic Correlate of Risk</td>
<td>KLD, RTB</td>
<td>803</td>
<td>up to 86%</td>
</tr>
<tr>
<td>WHIP3TB (IIb)</td>
<td>KNCV</td>
<td>2017-current</td>
<td>A randomised, pragmatic, open-label trial to evaluate the effect of three months of high-dose rifapentine plus isoniazid administered as a single round or given annually in HIV-positive individuals</td>
<td>RTB, TMB</td>
<td>893</td>
<td>up to 99.9%</td>
</tr>
<tr>
<td>3HP-DTG-DDI (III)</td>
<td>Unitaid/JHU</td>
<td>2018-current</td>
<td>Safety, tolerability, and drug-drug interactions of short-course treatment of latent tuberculosis infection with high-dose rifapentine and isoniazid among HIV-infected patients taking dolutegravir-based antiretroviral treatment</td>
<td>TMB</td>
<td>61</td>
<td>100%</td>
</tr>
<tr>
<td>A5300B/3220 3B/PHOENIx (III)</td>
<td>ACTG</td>
<td>2019-current</td>
<td>Protecting Households On Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients (PHOENIx MDR-TB)</td>
<td>RTB</td>
<td>0</td>
<td>n/a</td>
</tr>
</tbody>
</table>

### TB Vaccine Trials

<table>
<thead>
<tr>
<th>Study/Trial (Phase)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Aurum 102/THYB-05 (II)</td>
<td>EDCTP</td>
<td>2011-2012</td>
<td>Phase II Double-Blind, Randomized, Placebo-Controlled Study to Evaluate The Safety and Immunogenicity Of H1/Ic31®, an Adjuvanted Tb Subunit Vaccine, In HIV-Infected Adults With CD4+ Lymphocyte Counts Greater Than 350 Cells/mm3</td>
<td>TMB</td>
<td>24</td>
<td>99%</td>
</tr>
<tr>
<td>AERAS - GSK TB018 (IIb)</td>
<td>AERAS/GSK</td>
<td>2014-2018</td>
<td>A Phase Iib, Double-Blind, Randomised, Placebo-controlled study to evaluate the Efficacy, Safety and Immunogenicity of GSK Biologicals’ Candidate Tuberculosis (TB) Vaccine GSK 692342 against TB Disease, in Healthy Adults Aged 18-50 years, living in a TB Endemic Region</td>
<td>KLD, TMB</td>
<td>377</td>
<td>up to 95%</td>
</tr>
<tr>
<td>AERAS C037-456 (I)</td>
<td>AERAS</td>
<td>2015</td>
<td>A Phase I, Double-blind, Randomized, Placebo-controlled, Dose-escalation Study To Evaluate the Safety and Immunogenicity of AERAS-456 in HIV Negative Adults Successfully Treated for Drug-susceptible Pulmonary Tuberculosis</td>
<td>TMB</td>
<td>6</td>
<td>100%</td>
</tr>
</tbody>
</table>

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## Annexure 6: Aurum Clinical Trial Projects (2012 - present)

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<tbody>
<tr>
<td>AERAS-A055 (II)</td>
<td>AERAS</td>
<td>2019-Current</td>
<td>A Phase 2, Double-blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of H56:IC31 in Reducing the rate of TB Disease Recurrence in HIV Negative Adults Successfully Treated for Drug-Susceptible Pulmonary Tuberculosis</td>
<td>KLD, TMB</td>
<td>129</td>
<td>96%</td>
</tr>
<tr>
<td>MESA-TB</td>
<td>Gates MRI</td>
<td>2019-Current</td>
<td>A Phase 2, Double-blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of H56:IC31 in Reducing the rate of TB Disease Recurrence in HIV Negative Adults Successfully Treated for Drug-Susceptible Pulmonary Tuberculosis</td>
<td>KLD, TMB</td>
<td>86</td>
<td>99%</td>
</tr>
<tr>
<td><strong>TB Treatment Trials</strong></td>
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</tr>
<tr>
<td>NC002 (II)</td>
<td>TB Alliance</td>
<td>2012-2013</td>
<td>A Phase II Open-Label Partially Randomized Trial to Evaluate the Efficacy, Safety and Tolerability of the Combination of Moxifloxacin Plus PA-824 Plus Pyrazinamide After 8 Weeks of Treatment in Adult Patients With Newly Diagnosed DS or MDR, Smear-Positive Pulmonary Tuberculosis</td>
<td>TMB</td>
<td>7</td>
<td>98%</td>
</tr>
<tr>
<td>MAMS-TB-01 (II)</td>
<td>PanACEA</td>
<td>2013</td>
<td>A multiple arm, multiple stage (MAMS), phase 2, open label, randomized, controlled clinical trial to evaluate four treatment regimens including SQ109, two increased doses of rifampicin, and moxifloxacin in adult subjects with newly diagnosed, smear-positive pulmonary tuberculosis</td>
<td>TMB</td>
<td>15</td>
<td>100%</td>
</tr>
<tr>
<td>NC005 (II)</td>
<td>TB Alliance</td>
<td>2014-2015</td>
<td>A Phase 2 Open-Label Partially Randomized Trial to Evaluate the Efficacy, Safety and Tolerability of Combinations of Bedaquiline, Moxifloxacin, PA-824 and Pyrazinamide During 8 Weeks of Treatment in Adult Subjects With Newly Diagnosed Drug-Sensitive or Multi Drug-Resistant, Smear-Positive Pulmonary Tuberculosis</td>
<td>TMB</td>
<td>14</td>
<td>100%</td>
</tr>
<tr>
<td>NC006 (III)</td>
<td>TB Alliance</td>
<td>2015-2017</td>
<td>A Phase 3 Open-Label Partially Randomized Trial to Evaluate the Efficacy, Safety and Tolerability of the Combination of Moxifloxacin Plus PA-824 Plus Pyrazinamide After 4 and 6 Months of Treatment in Adult Subjects With Drug-Sensitive Smear-Positive Pulmonary Tuberculosis and After 6 Months of Treatment in Adult Subjects With Multi-Drug Resistant, Smear-Positive Pulmonary Tuberculosis.</td>
<td>KLD, RTB, TMB</td>
<td>42</td>
<td>up to 100%</td>
</tr>
<tr>
<td>TB-HDT (II)</td>
<td>BMGF</td>
<td>2016-2018</td>
<td>A Phase 2, Randomized, Open-Label Trial to Evaluate the Safety, Preliminary Efficacy, and Biomarker Response of Host Directed Therapies added to Rifabutin-modified Standard Antimicrobial Therapy in Adult Patients with Drug-Sensitive Smear-Positive Pulmonary Tuberculosis (TB HDT)</td>
<td>TMB</td>
<td>105</td>
<td>96%</td>
</tr>
<tr>
<td>SUDOCU</td>
<td>PanaCEA</td>
<td>2021-Current</td>
<td>A Phase IIIB, Open-Label, Randomized Controlled Dose Ranging Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Exposure-Response Relationship of different doses of Sutezolid in combination with Bedaquiline, Delamanid and Moxifloxacin in Adult Subjects with Newly Diagnosed, Uncomplicated, Smear-Positive, Pulmonary Tuberculosis</td>
<td>TBM</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td><strong>COVID Vaccine Trials</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ensemble 2</td>
<td>Janssen</td>
<td>2021-Current</td>
<td>A Randomized, Double-blind, Placebo-controlled Phase 3 Study to Assess the Efficacy and Safety of Ad26.COV2.S for the Prevention of SARS-CoV-2-mediated COVID-19 in Adults Aged 18 Years and Older</td>
<td>PTA</td>
<td>256</td>
<td>96%</td>
</tr>
</tbody>
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<th>CRS</th>
<th>Enrolled</th>
<th>Retained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novavax</td>
<td>Novavax, Inc.</td>
<td>2020-2021</td>
<td>A phase 2a/b, randomized, observer-blinded, placebo-controlled study to evaluate the efficacy, immunogenicity, and safety of a sars-cov-2 recombinant spike protein nanoparticle vaccine (sars-cov-2 rs) with matrix-m1™ adjuvant in South African adult subjects living without HIV, and safety and immunogenicity in adults living with HIV</td>
<td>PTA</td>
<td>122</td>
<td>97%</td>
</tr>
<tr>
<td>Ubuntu</td>
<td>SAMRC</td>
<td>2021-2021</td>
<td>Multi-Center, Randomized, Efficacy Study of an Early vs Deferred mRNA COVID-19 Vaccine in Regions with SARS-CoV-2 Virus Variants.</td>
<td>KLD, RTB, TMB</td>
<td>In screening</td>
<td></td>
</tr>
</tbody>
</table>

### COVID Prevention & Treatment Trials

<table>
<thead>
<tr>
<th>Study/Trial (Phase)</th>
<th>Sponsor Network</th>
<th>Duration</th>
<th>Study Description</th>
<th>CRS</th>
<th>Enrolled</th>
<th>Retained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crown Coronation</td>
<td>Wits</td>
<td>2020-2021</td>
<td>An international, Bayesian platform adaptive, randomized, placebo-controlled trial assessing the effectiveness of candidate interventions in preventing COVID-19 disease in healthcare workers</td>
<td>TMB</td>
<td>520</td>
<td>100%</td>
</tr>
<tr>
<td>C3RCT</td>
<td>UCT</td>
<td>2020-2021</td>
<td>The C3 Nitazoxanide for mild to moderate COVID-19 in HIV infected and HIV-uninfected adults with enhanced risk: a double-blind, randomised, placebo-controlled trial in a resource-poor setting (Catalysing the Containment of COVID-19; the C3-RCT) RCT</td>
<td>TMB</td>
<td>76</td>
<td>100%</td>
</tr>
<tr>
<td>ACTIV</td>
<td>ACTG/PPD</td>
<td>2021-2021</td>
<td>Adaptive Platform Treatment Trial for Outpatients with COVID-19 (Adapt Out COVID)</td>
<td>KLD, RTB, TMB</td>
<td>8</td>
<td>100%</td>
</tr>
</tbody>
</table>
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“To seek, to find, to share, to care.”

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