[redacted] [redacted]

Mentor Statement for [redacted] Gilead HIV Research Scholars Application

September 2nd, 20[redacted]

Dear Reviewer Committee Members,

We are pleased to express our firm commitment as co-mentors of Dr. [redacted] in support of her Gilead HIV Scholars grant application titled '[redacted].' Dr. [redacted] is an outstanding emerging investigator in HIV and [redacted] in low-resource settings. She is carving out an innovative research trajectory and is poised to become a leader in the field.

Dr. [redacted] has received exceptional training and experience in research and global health. She earned her medical degree with Distinction in Clinical and Translational Research at the [redacted]). As a medical student, she was awarded a [redacted] Research Fellowship, enabling her to spend a year in [redacted] – researching the integration of [redacted] screening into HIV care clinics. She subsequently earned a master's degree in Public Health from [redacted] with a concentration in Epidemiology and Biostatistics before training in [redacted]. Following her residency, she joined the Center for [redacted] at [redacted] as a postdoctoral research fellow before joining the faculty at the [redacted]). As a fellow, Dr. [redacted] was exceptionally productive, conceptualizing and launching a clinical trial in [redacted] that was among the first to report precancer treatment outcomes following [redacted] among HIV+ women in low-resource settings. During several trips to [redacted], in partnership with the County government and local stakeholders, she led the formation of the [redacted], which advises County leadership on implementing evidence-based prevention strategies. She published five first- or last-author manuscripts from her work, several abstracts were accepted to national and international meetings, and successfully competed for grants to fund her research. Awarded grants include the [redacted] Pilot Award, the [redacted] Investigator Award, the [redacted] Scientist Award, and the [redacted] Fellowship.

Dr. [redacted] was recruited to a tenure-track position at [redacted] through an internal K-12 program funded by the NIH's National Institute of Child Health and Human Development (NICHD), with 75% protected time and seed funding for research and professional development. Although she has been junior faculty at [redacted] for less than a year, she has conceptualized and developed two research protocols: 1) [redacted], and 2) [redacted]. In addition, she has successfully competed for grant funding both internally through the [redacted] Center and the [redacted], and through the NIH, where she is a co-investigator in the NIH [redacted], for which [redacted] is a research base. The [redacted] Network will conduct pragmatic clinical trials evaluating the effectiveness of clinically proven interventions to optimize [redacted] prevention among women living with HIV in LMICs and regions with health disparities in the United States.

For this Gilead HIV Scholars Program, Dr. [redacted] proposes an innovative and relevant study investigating whether topical Artesunate may be a safe and clinically effective neoadjuvant treatment for HIV-positive

women in LMICs who face long wait times to receive definitive treatment. This research has high relevance for women with HIV, both in LMICs and in rural parts of the United States, who also face barriers to accessing surgical treatment. Below, we summarize our qualifications as mentors and our mentoring plan. We are committed to Dr. [redacted]'s success in the proposed study, her career, and her transition to research independence.

[redacted] MD, MPH

I am a Professor of [redacted] School of Medicine. I have extensive experience in leading qualitative, quantitative, and translational research in reproductive infectious diseases, particularly in HPV and HIV. My research in HIV has included studies on reproductive health decision-making, acceptability of HIV testing, and stigma experienced by HIV-infected women. I am a member of the Women's Interagency HIV Study HPV working group and the Department of Health and Human Services Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Specific to Dr. [redacted]'s proposed research, I have more than 12 years of experience leading NIH- and industry-funded clinical trials on topical therapies for cervical precancer treatment in the U.S. I have led several studies on medical therapies for cervical precancer, including a randomized trial in [redacted] that demonstrated the safety and efficacy of [redacted]) for primary treatment of cervical intraepithelial neoplasia grade 2. I currently lead or co-lead several NIH- and industry-funded trials on medical therapies for [redacted], including being the co-Principal Investigator of an ongoing NIH/NCI-funded study of the feasibility of [redacted] in South Africa.

The potential for effective, accessible, patient-administered medical therapies as neoadjuvant, primary, or adjuvant therapy for cervical precancer is particularly profound in sub-Saharan Africa (SSA), highlighting the urgency of Dr. [redacted] planned study. Artesunate is an attractive agent to study for this purpose, given the decades of safety data for use in humans for malarial treatment and its ready availability in Africa. Additionally, this agent had clinically relevant efficacy results among HIV-negative women with cervical precancer in a U.S-based Phase I study, and is currently under investigation in a randomized Phase II study in the same population. If Dr. [redacted]'s study confirms safety for intravaginal use for both HIV-positive and HIV-negative women in SSA (Aim 1) and shows clinical signals of efficacy in HIV-positive women (Aim 2 and planned Aim 3 analyses), she will be well poised to perform a randomized Phase II efficacy study with likely support from the National Cancer Institute (NCI) for whom studies on topical therapies for cervical precancer is a priority area. Through my work in this field, I have developed relationships with the NCI and key NIH program officers. I will leverage both while mentoring Dr. [redacted]'s as she not only develops her protocol for this study, but also for future funding applications to ensure scientific rigor and competitiveness.

Dr. [redacted] joined the faculty at [redacted] last fall. I enthusiastically helped recruit her from the [redacted]. We currently meet biweekly to review her research agenda, grant and manuscript writing, study design and protocol development and implementation, and career planning. As part of her training plan, Dr. [redacted] will visit our 5-FU clinical trial site in South Africa during the first year of her award, where she will gain more exposure to several aspects of randomized interventional trials, including regulatory requirements, protocol development, and safety assessments. As a co-mentor on this study, I look forward to working closely with Dr. [redacted], her other mentor currently at [redacted] who has significant global health experience. Together our complementary expertise will help ensure Dr. [redacted]'s success. Of note, Dr. [redacted] was my mentor as a Reproductive Infectious Disease fellow at [redacted], and we have an excellent working relationship.

[redacted], MD, MPH

I am equally enthusiastic about serving as Dr. [redacted]s co-mentor for the Gilead HIV Scholars grant application. I have supported Dr. [redacted] for more than 14 years, having met her as a first-year medical student at [redacted]. In addition, I served as her primary mentor during her medical school research year and during her research fellowship at [redacted]. My track record in HIV and global health research, NIH funding, and success with prior trainees, as well as my longstanding commitment to Dr. [redacted]'s career, make me exceptionally qualified to co-mentor Dr. [redacted] on the proposed study.

I am a Professor in the Department of [redacted] and Principal Investigator of the [redacted] funded by the NIH. I conduct research in HIV/AIDS care and prevention in low-income countries and the HIV/AIDS intersection with sexual and reproductive health, including contraception and cervical cancer prevention. I lived and worked in Kenya between 1994 and 2002, where a majority of my global health research is based. Starting in 2004, alongside Dr. [redacted] – who is Dr. [redacted] in-country collaborator, I was the Principal Investigator of the [redacted] program that provided HIV treatment and prevention services to more than 53,000 HIV-infected persons at 72 health facilities in western Kenya. [redacted] has served as the foundation for more than 20 clinical and implementation research studies which I led or co-led, including those funded by NIH (NIAID, NCI, NIMH, OAR, FIC) and the [redacted]. I continue to co-lead several NIH-funded studies in western Kenya, whose infrastructure Dr. [redacted] will leverage for her proposed work. I have a strong track record of mentoring junior investigators to independence. Over the last three decades, I have directly mentored more than 60 doctoral/professional students, residents, and postdoctoral fellows and served as the primary mentor or co-primary mentor for 14 junior faculty on their NIH career development awards, most of whom have achieved research independence. I look forward to bringing my expertise to co-mentor Dr. [redacted], alongside Dr. [redacted], my former fellow and now a leader in investigating the use of topical therapies for cervical dysplasia treatment in the United States. Specific to Dr. [redacted] proposed research, I have extensive experience in the development of technologies to prevent HIV and reproductive health infections in the U.S. and Africa. I led a Phase 1 microbicide trial on [redacted], and a [redacted] among women at high risk of HIV acquisition in Durban, South Africa. My team and I published results from the [redacted]. My experiences will help ensure the success of Dr. [redacted]'s study and support her ability to leverage the findings of her planned Phase I study into a Phase II randomized study with successful grant funding.

In summary, Dr. [redacted] is an exceptional candidate for this award, and we are incredibly enthusiastic about mentoring her during the planned study. We have no doubt she will obtain important preliminary data from this award and will leverage it to support her transition to research independence. We firmly believe she will be a leader in her field.

Sincerely,

[redacted]

[redacted]

[redacted]

[redacted]

Mentoring Plan

Eligibility
Dr. Chemtai Mungo is a tenure-track Assistant Professor in the first year of her appointment. She has not received R01 funding.

1. Mentor Roles: As Chemtai's co-mentors, we commit to joint monthly virtual meetings during her award, including more regular meetings as needed during the Protocol development and study initiation phases. During these meetings, we will review the clinical trial design and endpoints, regulatory review processes both in the United States (where Dr. Rahangdale has significant experience with topical therapy) as well as in Kenya (where Dr. Cohen has significant experience with interventional trials of biologic agents including vaginal microbicides for HIV prevention), and ensure Chemtai is able to meet her planned timeline. We will work with Chemtai to develop an Individual Development Plan (IDP), which we will use to track progress on her training and research goals for this study and resulting abstracts, manuscripts, and future grants. We commit to reviewing her abstracts and manuscripts and guiding her as she identifies key national and international conferences to present her work to maximize dissemination, impact and future collaborations. We will mentor Chemtai when she writes her R01 and other potential future grants based on this work. Chemtai and Dr. Rahangdale are both based at the UNC-Chapel Hill campus, have offices in the same building, and both take hospital call at the UNC-CH hospital. As such, they will have multiple opportunities for in-person meetings and discussions concerning her research goals. Dr. Cohen's research in Kenya is primarily based in western Kenya in collaboration with Dr. Elizabeth Bukusi – who is Chemtai's in-country collaborator. Dr. Cohen spends approximately eight weeks a year in Kenya and will meet with Chemtai in person when they are both in-country. Of note, Chemtai's proposed study will recruit participants in Ministry of Health HIV clinics in western Kenya, where Dr. Cohen and his collaborators at the Kenya Medical Research Institute (KEMRI) have several ongoing NIH-funded HIV studies. As such, Chemtai will be able to leverage Dr. Cohen's and Dr. Bukusi's research infrastructure in Kenya through KEMRI, including administrative personnel, human resources, regulatory review support, and access to state-of-the-art KEMRI laboratories that have supported numerous clinical trials including HIV microbicide trials.

For the planned future immunology and microbiome analyses of cervicovaginal samples from this study (Aim 3), I (Dr. Cohen) have connected Chemtai with my long-term collaborators, Professor Omu Anzala (Professor of Medical Microbiology at the University of Nairobi and Director of the Kenya AIDS Vaccine Institute) and Dr. Lyle McKinnon (Associate Professor of Medical Microbiology and Infectious Diseases at the University of Manitoba with a joint appointment at the University of Nairobi. Professor Anzala and McKinnon both have over twenty years of experience in studying mucosal immunology as it relates to HIV transmission in the female reproductive tract and run an active NIH-funded microbiology lab at the Kenya AIDS Vaccine Institute in Nairobi, that will store the study specimens and perform future analyses.

2. Travel: To support Chemtai's travel to national and international conferences to present her work and cultivate potential collaborators, her department supports her travel to meetings as part of her start-up funds. In the coming year, Chemtai will attend the World Cancer Congress (where she is invited to speak as a Young Global Cancer Leader), the 18th International Conference on Malignancies in HIV/AIDS meeting, and the International Human Papillomavirus Conference, where she will be presenting her research.

Research Resources and Facilities

Funding: Chemtai is funded by a K12 career development award which provides 75% protected time for research on HIV and cervical cancer. With her clinical time limited to three months of the year, Chemtai spends approximately six months of the year abroad at her research sites, directly conducting and supervising her research, as well as teaching medical students and residents in Kenya and Malawi. Together with the K12, her ongoing research is funded by a Pilot Award from the UNC Center for AIDS Research. The funding from Gilead will allow Dr. Mungo to expand her current research on topical therapies by investigating a new topical therapy that can potentially move to a Phase II study.
UNC Facilities, Resources & Scientific Environment: UNC thrives in research and is ranked 5th for federal funding among U.S. universities. Particularly relevant to this application are the U.S. News and Report rankings for the UNC School of Public Health (#2; #1 in public schools) and the School of Medicine (#23 in

research). UNC also has a robust Global Health program with full-time faculty living in Malawi, Zambia, South Africa, Vietnam, and China. At UNC, Chemtai's work will be supported by the Institute for Global Health and Infectious Diseases (IGHID). The Institute coordinates activities related to patient care, basic and clinical research, and educational programs across North Carolina and at research and clinical sites in ten countries where UNC works, including Kenya. The IGHID has an outstanding regulatory group that manages ethics submissions with the University and SOM ethics committees, ethics committees, and Ministries of Health in host countries and investigational new drug (IND) and other submissions to the FDA and other regulatory authorities. In addition to IGHID, Chemtai's work is supported by the Lineberger Comprehensive Cancer Center (LCCC). As a faculty member of the LCCC, Chemtai will receive administrative and regulatory support from the Clinical Protocol Office (CPO) at LCCC in protocol development, including all biostatistical support for all the statistical needs related to the planned Phase I trial as well as regulatory support to enable successful initiation and completion of the trial. This support is provided at no cost as part of faculty development at UNC. Of note, the LCCC portfolio of phase I clinical trials includes several first-in-human evaluations of new anticancer compounds.

Kenya Facilities, Resources, & Scientific Environment:
Chemtai's study will be in collaboration with the Kenya Medical Research Institute (KEMRI) – see the letter of collaboration from Dr. Elizabeth Bukusi, a long-term mentor of Chemtai and the Chief Research Officer at KEMRI.

Scientific Environment: KEMRI is the national body responsible for carrying out health research in Kenya and is a leading center of excellence in health in Africa with more than 30-year history of successful HIV research in western Kenya – the site of Chemtai's proposed work. Prior HIV studies led by KEMRI and Dr. Bukusi include clinical trials in the prevention of mother-to-child HIV transmission (Kisumu Breastfeeding Study), HIV treatment as prevention (HIV Prevention Trials Network Study 052), the Vivagel microbicide study funded by the Consortium for National Health Research, giving rise to a team of very experienced biomedical and social scientists. All the KEMRI personnel who will support this study have vast experience working in clinical trials conducted within KEMRI, including in microbicide clinical trials. Relevant KEMRI expertise includes collaborative development and evaluation of vaginal products such as microbicide or diaphragms; assessment of product adherence, optimization of participant retention and follow-up, development of standard operating procedures, staff training manuals, GCP-compliant interview tools, and informed consent forms; training and oversight of staff to ensure that participant safety and rights are upheld all the time; scientific writing and results dissemination. Similar to prior studies she has performed with KEMRI, Chemtai will leverage this scientific environment to support the implementation of this study.

Laboratory: The state-of-the-art, ISP-accredited KEMRI molecular laboratory in western Kenya is located at the Centre for global health research campus at Kisian in Kisumu. The Kisian laboratory occupies 4,800 square feet of space with customized sections for the different assays, including the early infant HIV diagnosis, the sequencing, and bioinformatics section, which supports HIV drug resistance tests for individual patients and national HIV drug resistance surveys. The laboratory is currently the WHO national and regional laboratory for HIV drug resistance surveillance studies and utilizes both an in-house platform and FDA approved ViroSeq systems. The HIV viral load section is also housed in the molecular lab and has an average yearly turnover of 48,000 tests. This section serves to support various research studies as well as routine management of patients in western Kenya. The unit also has the capacity for NAAT screening testing. Additional facilities within the molecular laboratory include STI and HIV diagnosis, which includes capacity for laboratory incidence assays. The laboratory also has the capacity for sample storage with several freezers, two large cold rooms with automated temperature monitoring systems, office space for analysis, and six shared conference rooms, some with fully equipped video conferencing equipment.

Clinical: KEMRI has over 15-year history of supporting and building the local capacity for comprehensive, high-quality HIV service delivery in Ministry of Health clinics in western Kenya. The KEMRI program supports support 72 government health facilities providing HIV prevention, care, and treatment per the Kenya National Guidelines and includes the core services program areas: HIV testing and counseling, Prevention of Mother to Child Transmission (PMTCT), Voluntary Medical Male Circumcision (VMMC), and HIV care and treatment

services. Embedded within HIV care provision are numerous KEMRI-led research studies, many funded by the NIH, that recruit HIV-positive participants from the Ministry of Health clinics.

Office: The KEMRI research building is located in Kisumu town and was the site for the recently concluded HIV Pre-Exposure Prophylaxis (PrEP) trial. It comprises four clinical rooms where consenting, and interviewing can be carried out confidentially. Other facilities include an administrative office, an access-controlled data storage room, a laboratory, an open reception area, and bathroom facilities for both staff members and participants. In addition, the office has a photocopying machine and a secure server. The data room has several metallic and wooden lockable cabinets available in the data room and will be ideal for storing data containing identifiers.

Other: Administrative, regulatory, grants management, and procurement activities are supported through KEMRI, which currently has about 400 employees and manages around 200 active grants, including several from the NIH. Research is subject to review and approval by the KEMRI Scientific Ethics Review Unit (SERU) that maintains Federal Wide Assurance (FWA00002066).