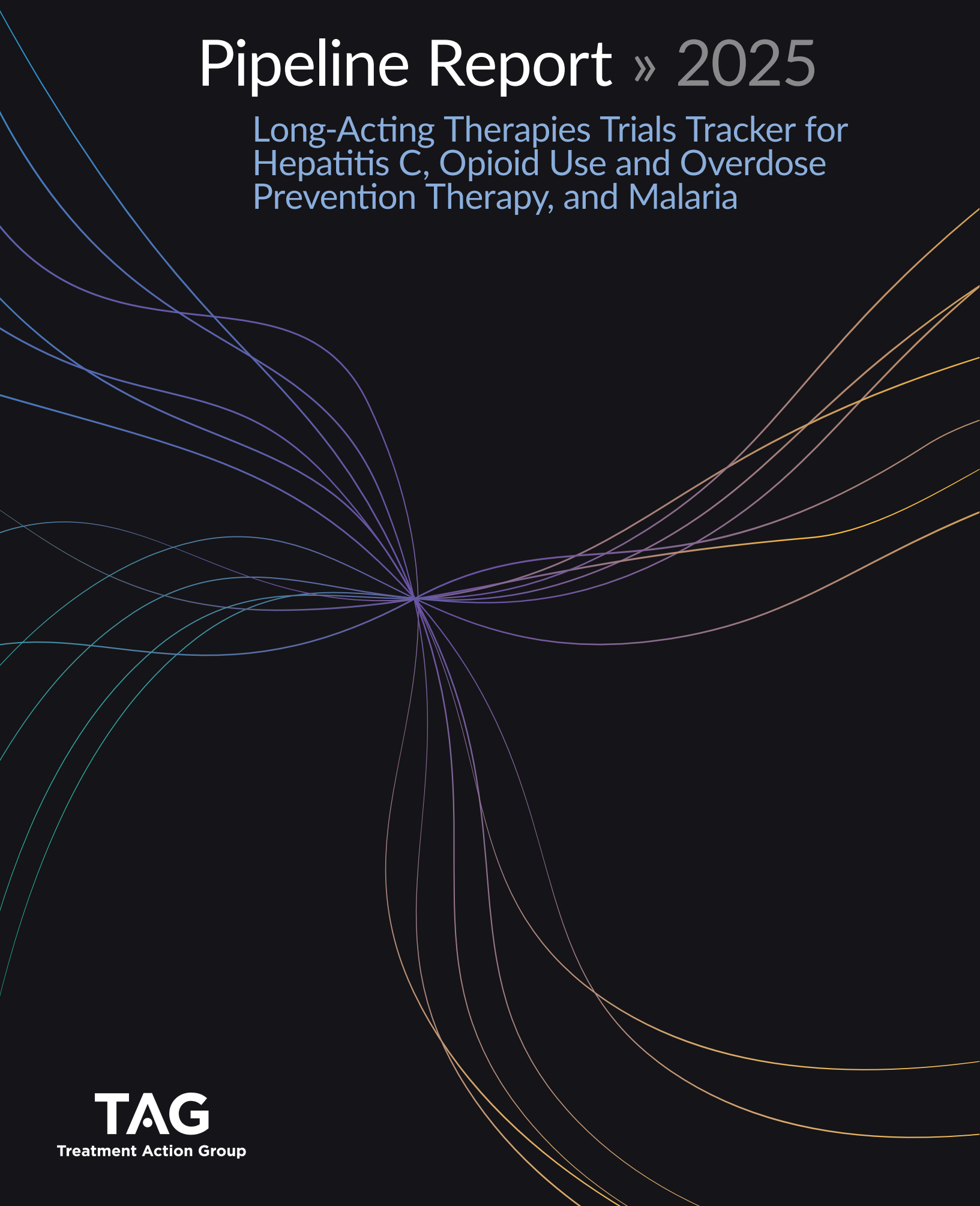
Pipeline Report » 2025

Long-Acting Therapies Trials Tracker for Hepatitis C, Opioid Use and Overdose Prevention Therapy, and Malaria



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Treatment Action Group

Long-Acting Therapies Trials Tracker for Hepatitis C virus, Malaria and Opioid Use and Overdose Prevention

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Biomedical innovations have always lingered as simple news headlines — and even sounded like fairy tales — to many in low-and middle-income countries (LMICs) for a few or even several years after their launch in high-income countries before becoming accessible. It took more than a decade from the introduction of effective combination antiretroviral therapy in high-income countries for them to become widely available in LMICs[1] and a worldwide campaign to reduce prices and establish new funding mechanisms to support their delivery.[2]

Currently, glecaprevir/pibrentasvir (G/P) and sofosbuvir/velpatasvir/voxilaprevir, two second-line direct acting antiviral (DAA) combinations recommended for retreatment of hepatitis C virus (HCV) following treatment failure[3] are not registered in most LMICs despite being approved by the U.S. Food and Drug Administration (FDA) in 2017.[4] Thanks to multiple efforts by health activists, advocates, and scholars who fought hard to elevate the urgency of combating and overcoming global health inequities, international institutions like Unitaid, the Medicines Patent Pool (MPP), The Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund), Clinton Health Access Initiative (CHAI), and the President's Emergency Plan for AIDS Relief (PEPFAR) were created to address this global health tragedy by reducing the time lag between when health technologies become accessible in high-income countries and LMICs. As a result, cabotegravir long-acting (CAB-LA), the first long-acting HIV pre-exposure prophylaxis (PrEP) approved by the FDA, which is administered once every two months, was introduced in Zambia and Zimbabwe in 2024, two years after being launched in high-income countries.[5]

More recently, one month after FDA approved the first twice-yearly long-acting injectable PrEP lenacapavir in June 2025,[6] the Global Fund announced it had signed an access agreement with the manufacturer, Gilead Sciences, to procure lenacapavir for LMICs.[7] Despite the U.S government freeze on global health funding resulting in the decimation of programs like the United States Agency for International Development (USAID) and PEPFAR,[8] as well as programmatic reprioritization within the Global Fund, the latter is still working toward securing a first shipment and delivery of lenacapavir for PrEP in at least one African country by the end of 2025.[9]

Long-acting therapies (LATs) hold immense potential for enhancing treatment outcomes by improving treatment adherence; reducing dosing frequency, thus lessening the treatment burden; preventing relapses arising from treatment interruption in people with chronic conditions; ensuring more constant plasma levels in the bloodstream; improving quality of life by enabling greater choice and satisfaction; and addressing stigma, tablet/pill fatigue, and drug resistance. LATs might also reduce the frequency of patient visits for some health conditions, thereby freeing up healthcare staff and potentially reducing overall healthcare expenditures through improved disease management.[10]

The Unitaid-funded LONGEVITY project seeks to develop both long-acting rifapentine and isoniazid as a tuberculosis prevention therapy (TPT) and G/P for HCV cure in high volumes and at lower prices for LMICs. This will offer people with these chronic diseases, which require frequent oral intake of medicines over several months, a choice and an opportunity to replace these with alternative administration routes to promote global equity in access to LATs. Tuberculosis (TB) returned to being the world's leading cause of death from a single infectious agent in 2023,[11] and viral hepatitis and TB were the second leading causes of death from communicable diseases in 2022, after COVID-19.[12]

While preclinical research on these LATs is ongoing, the Long-Acting Technologies Community Advisory Board (LAT CAB), cofounded and cochaired by Treatment Action Group and AfroCAB Treatment Access Partnership, is engaging with the LONGEVITY researchers and communities in various countries to raise awareness about this promising endeavor, as community engagement will be critical to demand generation when these LATs become available. In addition, the LONGEVITY Consortium has conducted global surveys of end users,[13] healthcare providers,[14] and policymakers[15] to understand their preferences and the acceptability and challenges of LATs. The surveys compared oral tablets/pills to long-acting injections, implants, and microarray patches.

Based on these surveys, long-acting injectables ranked as the most preferred long-acting modality end users and clinicians would be willing to try. With respect to HCV, 78% of end users preferred an injectable long-acting formulation if this worked just as well as the currently available 12-weeks of daily oral pills/tablets that constitute the standard of care in LMICs,[16] while 64% of healthcare providers indicated that this long-acting modality would be preferred by end users if these were priced similarly to currently available DAAs.[17] With respect to TB, 75% of end users indicated they "definitely would try [a long-acting injectable],"[18] while 90% of healthcare providers expressed willingness to prescribe long-acting TPT if efficacy, safety, and cost were the same as oral tablets/pills.[19] The 2025 Tuberculosis Treatment Pipeline Report provides an overview of the state of the clinical TB treatment research pipeline, including long-acting TB therapies.[20]

This trials tracker, an update of the *2024 Long-Acting Therapies Trials Tracker for Hepatitis C, Opioid Use and Overdose Prevention Therapy, and Malaria Pipeline Report*,[21] provides a compilation of ongoing and recently completed clinical trials on LATs for HCV, opioid use and overdose prevention therapy, and malaria in the research and development pipeline. The trials in this tracker are listed on the World Health Organization (WHO) International Clinical Trials Registry Platform website, the Pan African Clinical Trials Registry, the European Union Clinical Trials Register, and the United States clinicaltrials.gov website.

The trial registry identifier numbers link directly to trial entries, which contain more detailed information on trial design, enrollment criteria, principal investigators, and locations. Please communicate directly with the contact listed in the individual trial registry entries for all information about the status of the research. These HCV, opioid use and overdose prevention, and malaria LATs clinical trials were compiled between June 2 and September 11, 2025, and will be updated on an annual basis. Please send updates, corrections, or suggestions to Joelle Dountio Ofimboudem at jdountio@treatmentactiongroup.org.

TABLE 1: Long-acting therapies for Hepatitis C, Malaria, and Opioid Use and Overdose Prevention in the research and development pipeline

	Other information	Trial registry identifier	Manufacturer/sponsor	Location	Phase	Status/Estimated completion date
Malaria						
A Phase 1b, Randomized, Double-Blind, Placebo-Controlled Trial to Assess the Safety, Tolerability, and Pharmacokinetics of monoclonal antibody L9LS in Infants in Mali and to Evaluate the Impact of L9LS on Subsequent R21/Matrix-MTM Vaccine Immunogenicity	Injectable Sample size: 120 Objective: to assess the safety, tolerability, and pharmacokinetics (PK) of L9LS in infants in Mali and to evaluate the impact of L9LS on subsequent R21/Matrix-MTM vaccine immunogenicity	NCT06461026	National Institute of Allergy and Infectious Diseases (NIAID) National Institutes of Health (NIH) University of Washington Harvard School of Public Health (HSPH) Indiana University School of Medicine, Indiana University	Mali	1	2025
Single Ascending Dose Study to Assess the Safety, Tolerability and Pharmacokinetics of MMV371 LAI in Healthy Participants (MV371 LAI FiH)	Depot injection Sample size: 24 Objective: to assess the safety, tolerability, and PK of a single intra-muscular depot injection of MMV371 long-acting injection (LAI) formulation in healthy participants.	NCT06558643	Medicines for Malaria Venture	United Kingdom	1	Recruiting
Single Ascending Dose Study to Assess the Safety, Tolerability and Pharmacokinetics of LAI MMV055 Alone and in Combination With MMV371 in Healthy Participants	Injectable Sample size: 72 Objective: to assess the safety, tolerability, and PK of a single dose of intramuscular (IM) depot injection(s) of LAI formulations of MMV055 administered alone (Part A) and in combination with MMV371 (Part B) in healthy participants.	NCT07011511	Medicines for Malaria Venture The Doctors Laboratory Ltd Quotient Sciences	United Kingdom	1	Recruiting
Single-Use Antimalarial Monoclonal Antibodies for Post-Discharge Malaria Prevention in Children with Severe Anaemia or Severe Malaria in Kenya: A Multi-Centre, Parallel-Group, Two-Arm Randomised Placebo-Controlled Non-Inferiority Trial	Injectable Sample size: 398 Objective: to assess the efficacy of a single dose of L9LS versus post-discharge malaria chemoprevention against microscopy or RDT-confirmed clinical malaria in hospitalized children with severe anemia or severe malaria by 6 months after investigational product administration	NCT07082205	Liverpool School of Tropical Medicine	Kenya	3	2027

	Other information	Trial registry identifier	Manufacturer/sponsor	Location	Phase	Status/Estimated completion date
A Randomized, Double-Blind, Placebo-Controlled Trial to Assess the Safety, Tolerability, and Efficacy of the Anti-Malaria Monoclonal Antibody L9LS in Infants 10 Weeks of Age in Western Kenya and to Evaluate the Impact of L9LS on Subsequent Malaria Vaccine Immunogenicity	Injectable Sample size: 326 Objective: to evaluate the safety, tolerability, PK, and efficacy of a one-time IM administration of the monoclonal antibody (MAb) L9LS to healthy Kenyan infants approximately 10 weeks of age, followed by an assessment of the impact of L9LS on the safety and immunogenicity of subsequent administration of the RTS,S/AS01 or R21/Matrix-MTM vaccine	PACTR202410517100221	Office of Clinical Research Policy and Regulatory Operations NIAID NIH	Kenya	2	2026
Hepatitis C Virus						
Nothing found						
Opioid use and Overdose prevention therapy						
A Phase II Multi-center Safety Study Examining the Use of the O'Neil Long-acting Naltrexone Implant (OLANI) in Opioid Dependent Persons Receiving Repeat Dosing	Implant (in abdominal region) Sample size: 250 Objective: to evaluate the safety profile and efficacy of the OLANI when used in participants who meet the diagnosis of opioid use disorder and who will be voluntarily seeking relapse-prevention treatment using the naltrexone (NTX) implant	NCT05382091	National Institute on Drug Abuse (NIDA) New York State Psychiatric Institute Columbia University The Emmes Company, LLC University at Buffalo Go Medical Industries Pty Ltd	United States	2	2029
A Randomized Controlled Trial Examining Extended-Release Injectable Buprenorphine in Those Who Use High Potency Synthetic Opioids	Injectable Sample size: 60 Objective: to compare buprenorphine formulations (sublingual buprenorphine versus long-acting injectable buprenorphine) for treating opioid use disorder among individuals who use fentanyl and/or other high potency synthetic opioids	NCT06726200	Rachel R. Luba NIDA	United States	Early phase 1	2029

	Other information	Trial registry identifier	Manufacturer/sponsor	Location	Phase	Status/Estimated completion date
A Randomized, Comparator-Controlled, Multiple Dose-Level Study Evaluating the Pharmacokinetics and Safety of BIOPIN (Naltrexone) Implants Compared to Monthly Vivitrol Injections in Healthy Adults Over a 12-Month Period	Implant Sample size: 33 Objective: to see what the blood levels of naltrexone are from two different doses of the BIOPIN implant over time and to compare it to blood levels of naltrexone from Vivitrol®, an FDA-approved injectable form of extended-release naltrexone given once a month	NCT07064564	Akyso Pharmaceuticals NIDA Cenexel JBR Fast-Track Drugs & Biologics, LLC Aliri Bioanalysis Ardena Element Analytics	United States	1	2027
The Impact of Intraoperative Methadone on Postoperative Opioid Use	Injectable Sample size: 200 Objective: to assess the effectiveness of intraoperative methadone on postoperative opioid use, pain control, and recovery in patients undergoing autologous breast reconstruction	NCT07092475	University of Utah	United States	3	2028
Evaluating Pain Control Strategies in Postpartum Patients on Opioid Use Disorder Medications: Efficacy and Safety Outcomes	Injectable Sample size: 20 Objective: to investigate the efficacy of three different modalities of postoperative pain control in patients with opioid use disorders.	NCT06617949	Medical College of Wisconsin	United States	Early Phase 1	2028
Anchoring Intermittent Long-acting Antimicrobials to Medication for Opioid Use Disorder Treatment to Facilitate Structured Transitions of Care for People Who Use Drugs Admitted to the Hospital with Invasive Infections	Injectable Sample size: 25 Objective: to determine the efficacy of an alternative strategy using intermittent outpatient oritavancin therapy dosed weekly combined with initiation and continuation of medication assisted treatment for opioid use disorder for completion of antimicrobial therapy in a 12 week prospective, open-label study	NCT05521880	University of Maryland, Baltimore	United States	4	2025

	Other information	Trial registry identifier	Manufacturer/sponsor	Location	Phase	Status/Estimated completion date
Comparative Effectiveness of Two Formulations of Buprenorphine for Treating Opioid Use Disorder in Veterans (VA-BRAVE)	Injectable and sublingual Sample size: 952 Objective: to determine whether a 28-day long-acting injectable subcutaneous formulation of buprenorphine is superior in retaining veterans in opioid treatment and in sustaining opioid abstinence compared to the daily sublingual buprenorphine formulation	NCT04375033	VA Office of Research and Development	United States	4	2025

L9LS is an investigational lab-made monoclonal antibody derived from a natural antibody developed by scientists at the NIH in partnership with the Medicines for Malaria Venture (MMV). L9LS targets and neutralizes Plasmodium falciparum parasites — a parasitic protozoan that causes the most severe and deadly form of human malaria — before they can infect the human liver and cause illness. By neutralizing these parasites, L9LS prevents them from reaching and infecting liver cells, thereby stopping the infection from developing.

R21/Matrix-MTM Vaccine is a malaria vaccine developed to prevent Plasmodium falciparum malaria, which is the deadliest form of the disease and is most common in Africa. It was developed by the University of Oxford in partnership with the Serum Institute of India and Novavax and is primarily intended for young children in malaria-endemic regions, particularly in sub-Saharan Africa.

MMV371 is a LAI antimalarial drug candidate developed by MMV in partnership with Scripps Research and Janssen Pharmaceuticals. It is designed to provide at least three months of protection against malaria with a single intramuscular injection. As a prodrug of the approved antimalarial drug atovaquone, MMV371 can circulate in the bloodstream for a significantly longer period compared to standard oral atovaquone. MMV371 is designed to be effective against both *Plasmodium vivax* and *Plasmodium falciparum*, the two most prevalent malaria parasites.

MMV055 is a potential new antimalarial drug candidate developed by MMV. MMV055 is being investigated as a potential partner drug for MMV371 to create a LAI for malaria prevention. MMV055 is intended to target multiple life stages of the malaria parasite, including liver (preerythrocytic), blood (asexual stage), and possibly vector stages.

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