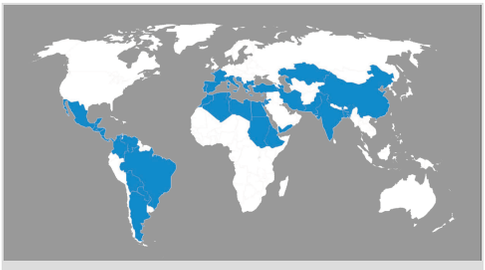
Background

Global Burden | Causative Agent & Transmission | Pathogenesis | Current Control Strategy | Existing Products | Get Involved

What is Leishmaniasis?

Leishmaniasis is a widespread parasitic disease transmitted by the bite of an infected sandfly. The disease occurs in three forms, cutaneous leishmaniasis, mucocutaneous leishmaniasis, and visceral leishmaniasis, each of which varies in incidence and severity. The three predominant forms of leishmaniasis can affect the skin, mucosa, and/or internal organs resulting in severe disfigurement, disability, or death.

Global Burden



Countries with areas of visceral and cutaneous leishmaniasis risk. Leishmaniasis epidemiological information has serious gaps. *(WHO, 2003)*

Leishmaniasis is endemic in 88 countries across 4 continents with approximately 350 million people currently at risk for infection.[1,2] Each year it is estimated that 1.6 million new infections occur as well as 47,000 deaths.

Leishmaniasis occurs in three forms that differ in incidence and geographic distribution as summarized in the table below.[2]

Disease Form	Infections (per year)	Geographic Distribution
Cutaneous leishmaniasis (CL)	1,100,000	90% of cases in Afghanistan, Algeria, Brazil, the Islamic Republic of Iran, Peru, Saudi Arabia, Sudan, and the Syrian Arab Republic
Mucocutaneous leishmaniasis (MCL)	35,000	90% of cases in Brazil, Peru, and the Plurinational State of Bolivia
Visceral leishmaniasis (VL)/Kala-azar	500,000	90% of cases in Bangladesh, Brazil, Ethiopia, India, Nepal, and Sudan

Organ damage and death associated with untreated visceral disease, as well as disfiguring damage to the mucosa and skin resulting from the mucocutaneous and cutaneous diseases, contribute to the morbidity associated with leishmaniasis. Morbidity as measured in DALYs across World Health Organization (WHO) regions are summarized in the table below.

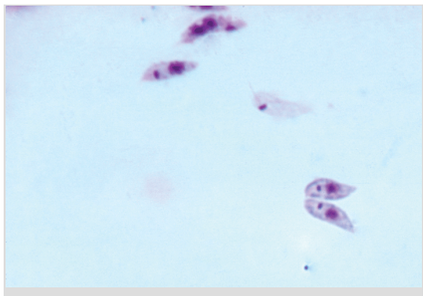
WHO Region	DALY (in thousands)[3]
Africa	328

Americas	45
Eastern Mediterranean	281
Southeast Asia	1,264
Western Pacific	51
Total:	**1,969**

The economic impact of leishmaniasis has not been estimated.

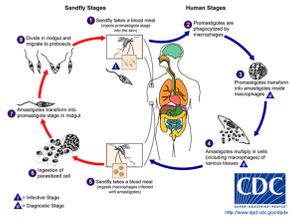
Back to Top

Causative Agent and Transmission



Leishmania donovani parasites
(photo: CDC)

Leishmaniasis is caused by protozoan parasites of the genus *Leishmania*. Upon taking a blood meal, an infected sandfly injects the leishmania parasites into the skin. The parasites are taken up by macrophages where they differentiate into an intracellular form, known as an amastigote, and replicate.



Leishmania spp. life cycle.
Click to view

Leishmania spp. parasites are all transmitted through the bite of sandflies of the genus *Phlebotomus* (Africa, Middle East, and Asia) or *Lutzomyia* (Americas). Sandflies become infected by taking up parasite infected macrophages when ingesting the blood of an infected host. Ingested parasites transform from the intracellular amastigote form to the extracellular promastigote form in the midgut of the fly before being transmitted via a subsequent blood meal. Interestingly, leishmaniasis is primarily a zoonosis; the majority of transmission occurs from infected animals to humans via the sandfly rather than from humans to humans. The large animal reservoir for leishmaniasis has implications for control strategies.

Pathogenesis

Cutaneous leishmaniasis is characterized by skin lesions that are formed at the site of initial infection by the sandfly bite. As parasites replicate inside and eventually lyse macrophages and endothelial cells in the skin, direct cellular damage occurs. There are over 15 species or subspecies of *Leishmania* parasites that cause cutaneous disease. Most cutaneous lesions heal slowly over the course of several months without medication. However, the open wounds associated with untreated disease leave the host susceptible to other infections.

For unknown reasons, certain species of *Leishmania* parasites migrate beyond the site of initial sandfly bite to cause more extensive disease. Mucocutaneous disease occurs when parasites migrate to mucosal surfaces, generally of the nose or mouth. As with cutaneous lesions, parasites replicate in the tissues causing damage. However, unlike the cutaneous form of the disease, mucocutaneous lesions are not self-limiting and can result in permanent damage or loss of the nose, soft palate, or lips. Mucocutaneous disease is the least common form of leishmaniasis and is primarily limited to South America. The majority of disease is caused by a single subspecies of the parasite, *Leishmania baziliensis braziliensis*.

Following initial infection, a sub-set of parasite species can also migrate to organs throughout the body resulting in visceral leishmaniasis (also known as kala-azar). Severe damage to the liver and spleen commonly cause massive enlargement of these organs. Without treatment, death occurs within two years. The parasite species responsible for the majority of visceral disease vary geographically:

- Indian subcontinent and Africa: *L. donavani*
- Mediterranean: *L. infantum*
- Central and South America: *L. chagasi*

Back to Top

Current Control Strategy

Control strategies for leishmaniasis have been difficult. There are several factors limiting progress towards disease control:

- Large animal reservoir of parasites
- Growing sandfly resistance to common insecticides
- Bednets are only effective if frequently re-treated with insecticide as sandflies are significantly smaller than other insect vectors and can often pass through the mesh of untreated nets

Despite these challenges, the current control strategy for leishmaniasis includes:[1]

- Early diagnosis and prompt treatment of disease
- Vector control through indoor residual spraying and long-lasting insecticide treated nets (LLITN)
- Detection and containment of epidemics

Back to Top

Existing Products

Drugs

There are several drugs available for the treatment of leishmaniasis, but many of the newer medications are not yet available in all endemic areas. Drug resistance is a concern in regions using monotherapies for treatment.

Drug	Dosing	Availability	Comments
Pentavalent antimonials: Sodium stibogluconate, SSG Meglumine antimoniate	30+ days of IM or IV injections	All endemic regions	Toxic side effects and drug resistance are common
AmBisome®, liposomal amphotericin B	1-5 days IV injection	Approved in 1997 in US for VL Used in India to replace more toxic traditional formulation of amphotericin B Seeking registration and adoption in Africa with DNDi	
		Approved in India in 2003	

Miltefosine	28 days, oral	for VL Seeking registration and adoption in Africa with DNDi	Only oral drug for VL; side effects generally limited and include diarrhea or vomiting
Paromomycin	21 days, IM injection	Approved in 2006 in India for VL Seeking registration and adoption in Africa with iOWH and DNDi	

There is an intensive effort underway, primarily through DNDi, to register and encourage adoption of newer, safer visceral leishmaniasis medications outside of India. This is primarily being done through more extensive clinical trials of combination therapies of the drugs listed above.

Vaccines

There is currently no vaccine approved for the prevention of leishmaniasis.

Some informal vaccination efforts for the prevention of cutaneous leishmaniasis have been conducted in endemic areas through a process known as "leishmanisation." This process involves inoculating an area of skin (usually an area hidden by clothing) using live parasites from the active lesion of another person. Although difficult to standardize and extremely variable in outcome, this strategy does provide some protection.

Diagnostics

Several tests, including rapid tests for use at the point of care, are available for leishmaniasis.

Diagnostic Methods	Notes
Direct Agglutination Test (DAT)	High sensitivity including in HIV+ patients Specimen: Blood sample Kit contains freeze dried antigen for stability and long shelf life No refrigeration required Current gold standard for field diagnosis of VL
Kala-azar Latex Agglutination Test (KALtex)	High specificity, medium sensitivity Specimen: Urine sample Uses stable, non-protein antigen
RK39 Dipstick	High specificity, high sensitivity except in HIV + patients Detects species that cause VL (*L. donovani*, *L. infantum*, *L. chagasi*) Specimen: Blood sample Can be stored at room temperature
Culture/PCR	Highly specific, can determine species of parasite, low sensitivity depending on sample obtained Tissue samples (skin snip for CL or organ/bone marrow aspirate for VL)

	Parasites are detected by culture or PCR conducted on the sample Used as test of cure as antibodies detected by other tests can persist after treatment

Rapid tests of cure following treatment of VL that do not require difficult to obtain organ or bone marrow aspirate are still needed.

Back to Top

References

1. WHO Leishmaniasis, available here.
2. WHO (2010) First WHO report on neglected tropical diseases 2010: working to overcome the global impact of neglected tropical diseases.
3. WHO (2004) Global Burden of Disease.

Get Involved

To learn how you can get involved in neglected disease drug, vaccine or diagnostic research and development, or to provide updates, changes, or corrections to the Global Health Primer website, please view our FAQs or contact us at globalhealthprimer@bvgh.org.

Pipeline & Analysis

Drugs | Vaccines | Diagnostics | Get Involved

Drugs

PIPELINE

Back to Top

ANALYSIS

The primary focus of new drug development for leishmaniasis is improved efficacy and simplified treatment for visceral disease. It is possible that significant progress can be made through improving access to existing therapies and developing novel combination therapies that both reduce the risk for drug resistance and shorten treatment courses. In line with these priorities, the majority of clinical stage candidates in development for leishmaniasis include new combinations and new formulations of existing drugs. Efforts are also being directed towards expansion of registration and use of existing products.

There is only one new chemical entity (NCE) in clinical stage development for visceral leishmaniasis, sitamaquine. However, potential renal toxicity observed in a phase II trial has raised uncertainty regarding whether or not this product will remain in active development.

There is a greater diversity among programs in the pre-clinical and discovery stages of development for leishmaniasis. Novel oral formulations of amphotericin B are in development as are NCEs spanning several drug targets and classes of molecules (including DNA damage inducers, natural products, lipid biosynthesis inhibitors, boron based molecules, 2-quinoline analogs, and others). Establishment of novel oral combination therapies, preferably in short course single pill formulations, has the potential to replace both existing therapies and the combinations of injectable/oral therapies currently in development.

	Strengths	Weaknesses	Opportunities	Risks
Combination therapies (Multiple existing drugs)				
Most advanced program: Phase III	Reduced risk for drug resistance Potential to reduce treatment time and improve safety Based on extensively evaluated, approved single medications	Potentially involves complicated combinations of injections and oral drugs	Expansion of use of newer drugs from India to other parts of Asia, Africa, and Latin America Potential for future multi-drug, single formulations to simplify treatment	Potential oral treatments in pre-clinical and discovery stage development may eventually replace combinations of injectable drugs
New formulations (Existing drugs)				
Most advanced program: Amphomul, Phase III	New formulation of existing approved VL treatment Potential for single injection cure	Not orally available	Development of combination single injection cure	May not be an improvement over AmBisome, currently available injectable liposomal formulation of amphotericin B Oral formulations of amphotericin B in pre-clinical development may replace this product
8-aminoquinolines (Target unknown)				
Most advanced	Once daily oral dosing	Concern over possible	Development of	Will not be adopted until

program: Sitamaquine, Phase II	showed efficacy in phase II trial Only NCE in clinical development	renal adverse events	combination therapies with approved oral VL drug (Miltefosine)	at least as safe as on market products

Back to Top

Vaccines

PIPELINE

Product/Research Program	Developers	Discovery	Pre-clinical	Phase I	Phase II	Phase III
ACE527	Johns Hopkins Bloomberg School of Public Health PATH Pierrel Research USA TD Vaccines A/S					
dmLT	National Institute of Allergy and Infectious Diseases PATH Tulane University					
SBL 109	Crucell PATH					
Peru-15 pCTB (ETEC)	National Institute of Allergy and Infectious Diseases					
FTL-LTB chimera protein	Naval Medical Research Center Sanofi Pasteur University of Colorado					
LT/ST fusion proteins	International Enteric Vaccine Consortium PATH Research Council of Norway					
EtpA glycoprotein	University of Tennesee					
ACE920	TD Vaccines A/S					
SRP	Syntiron					
Mucosal immunobiology and vaccines discovery	Mucosal Immunobiology and Vaccine Center					
Mimopath-based ETEC vaccine	Mucosis B.V. PATH					

Traveler's diarrhea vaccine	Intercell AG					On Hold

Back to Top

ANALYSIS

Patients who have been treated and subsequently cured of leishmaniasis generally have strong protective immune responses towards the parasite. This suggests that development of a preventative vaccine should be possible. Furthermore, despite the diversity of parasite species that can cause leishmaniasis, serological differentiation of infection between different species has not been possible, thus suggesting a universal vaccine that can protect against multiple species is an achievable goal.

Development of whole cell, killed leishmania vaccines was pursued from the 1930s through the 1980s. The greatest success was observed in studies in Brazil and Iran in the 1980s where efficacy rates as high as 50% were observed.[1] Unfortunately, efficacy was highly variable across these studies, and ultimately these vaccine development programs were abandoned. Live vaccines are not being pursued at this point, although several factors may contribute to revisiting this approach along with whole cell, killed leishmania vaccines in the future, including:

1. Subsequent studies of the whole cell, killed vaccines as therapeutic, as opposed to preventive vaccines, showed improved efficacy when combined with therapeutics
2. New understanding of how human immune responses differ between sandfly delivered parasites and needle delivered parasites
3. Progress towards development and understanding of other whole cell, killed and live attenuated vaccines for parasitic diseases, such as malaria
4. Availability of improved adjuvants, which are more powerful than the BCG adjuvant used in these original studies.

The most advanced active vaccine development program for leishmaniasis is a series of recombinant protein vaccines in development by the Infectious Disease Research Institute (IDRI) in Seattle, WA. The protein antigen used in these vaccines is a combination of TSA, LmSTI1, and LeIF proteins from the parasite. The polyprotein antigen has been optimized slightly across three generations of this vaccine, called LEISH-F1 + MPL-SE (LEISH-111F + MLP-SE), LEISH-F2 + MPL-SE, and LEISH-F3 (the current active product). Clinical trials for the first and second generation vaccines were primarily carried out as therapeutic trials for CL or a condition known as post kala-azar dermal leishmaniasis (PKDL) that is characterized by parasite infection re-occuring in the skin after treatment of visceral disease. These particular clinical trial settings were evaluated in part to more rapidly assess efficacy of these vaccines. However, the ultimate goal of IDRI, and others working on leishmaniasis vaccine development, is to develop and obtain approval for a preventive vaccine for VL.

Other vaccines in pre-clinical development are exploring newer vaccine technologies such as peptide antigen vaccines, DNA vaccines, and viral vector vaccines. Many of these newer technologies are also being assessed as potential preventive vaccines for dogs, an important animal reservoir for *Leishmania* spp. parasites. Animal reservoir vaccination may serve as an interesting tool to evaluate the safety and efficacy of novel vaccine technologies as a precursor to human clinical trials.

Diagnostics

As there are now multiple leishmaniasis tools in the pipeline and available for diagnosis, even in resource poor settings, future development of diagnostics should focus on the identification of better endpoints and easier to obtain samples to test for cure in drug trials for VL. Bone marrow or organ tissue samples needed to detect cure after VL treatment are difficult and dangerous to obtain in a resource poor setting. Because of lasting immune responses following treatment, serological tests also cannot be used to detect cure. Therefore, simplified test of cure assays that can be performed in low resource settings represent the most immediate diagnostic need.

Back to Top

References

1. Modabber F (2010) Leishmaniasis vaccines: past, present, and future. *International Journal of Antimicrobial Agents* **36S**:

S58-S61.

Get Involved

To learn how you can get involved in neglected disease drug, vaccine or diagnostic research and development, or to provide updates, changes, or corrections to the Global Health Primer website, please view our FAQs or contact us at globalhealthprimer@bvgh.org.

Tools

The following series of tables describe the availability of tools for research, discovery, and development of novel drugs, vaccines, and diagnostics for leishmaniasis. The tools listed in the following tables are not intended to be an all-inclusive list but rather capture the most common tools used for drug, vaccine, and diagnostic development. The tools for leishmaniasis are generally well developed.

Drug Development Tools

Basic Research: Target Identification	Target Validation	Screening: Hit/Lead Identification Optimization	Pre-clinical Validation	Clinical Validation
Genome: Sequenced and annotated (*L. braziliensis*, *L. infantum, L. major,* and *L. Mexicana*) **Key databases:** TriTrypDB ***In vitro* culture*:*** Yes, *L. major* most common species used in laboratories	**Gene knock-outs:** Yes **Conditional gene knock-outs:** Yes **Transposon mutagenesis:** Possible **RNAi:** Yes **Other antisense technology:** Yes **Parasite viability assays:** Yes **Transcription microarrays:** Yes **Proteomics:** Yes **Crystal structures:** Yes	**Whole-cell screening assays:** Yes, limited relevance to human infection **Enzymatic screening assays:** Yes	**Animal models:** Yes, mouse, hamster, dog, and monkey models available	**Monitoring treatment efficacy:** Yes, but challenging for VL **Availability of endpoints:** Yes, clearance of parasitemia **Availability of surrogate endpoints:** No **Access to clinical trial patients / sites:** Yes

Back to Top

Vaccine Development Tools

Basic Research: Antigen Identification	Immune Response Characterization	Clinical Validation
See drug development tools above	**Predictive animal models:** Yes, no animal models exactly reproduce human response but mouse model and hamster model (better for VL) most commonly used	**Surrogate markers of protection:** No **Challenge studies possible:** Potentially, challenge studies using CL were

	Detection of endogenous antigen specific response in clinical samples: Yes, not fully characterized **Natural immunity well characterized:** No, natural immunity after parasite cure exists but is still the subject of study	performed in the 1980s, but not currently used

Back to Top

Diagnostic Development Tools

Basic Research: Biomarker Identification	Biomarker Validation	Clinical Validation
See drug development tools above	**Biomarkers known:** Yes **Access to clinical samples:** Yes **Possible sample types:** Blood, skin, organ, and bone marrow aspirate	**Access to clinical trial patients/sites:** Yes **Treatment available if diagnosed:** Yes

Get Involved

To learn how you can get involved in neglected disease drug, vaccine or diagnostic research and development, or to provide updates, changes, or corrections to the Global Health Primer website, please view our FAQs or contact us at globalhealthprimer@bvgh.org.

Back to Top

Product Details

ACE527

Synonyms:
ACE527

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:
Anti-toxin, LT

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Live attenuated vaccines

Mechanism of Action:

Molecule Class:

Administration Route:
Oral

Notes:

Clinical Trials:

NCT01060748
NCT00901654

Publications:

ACE920

Synonyms:
ACE920

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:
Preventive, cross protection for Campylobacter

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Unknown

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

dmLT

Synonyms:
dmLT

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:
Anti-toxin, LT

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:

Molecule Class:

Administration Route:
Oral

Notes:

Clinical Trials:

NCT01147445

Publications:

EtpA glycoprotein

Synonyms:
EtpA glycoprotein

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

FTL-LTB chimera protein

Synonyms:
FTL-LTB chimera protein

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

LT/ST fusion proteins

Synonyms:
LT/ST fusion proteins

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

Mimopath-based ETEC vaccine

Synonyms:
Mimopath-based ETEC vaccine

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:

Molecule Class:

Administration Route:
Oral

Notes:

Recombinant protein carried by bacterium-like particles (BLPs).

Clinical Trials:

Publications:

Mucosal immunobiology and vaccines discovery

Synonyms:
Mucosal immunobiology and vaccines discovery

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:
Preventive

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Unknown

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

Peru-15 pCTB (ETEC)

Synonyms:
Peru-15 pCTB (ETEC)

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:
Preventive, cholera vaccine with ETEC cross protection

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Live attenuated vaccines

Mechanism of Action:

Molecule Class:

Administration Route:
Oral

Notes:

In development for cholera but has potential ETEC cross protection.

Clinical Trials:

NCT00654108

Publications:

SBL 109

Synonyms:
SBL 109

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Inactivated vaccines

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

SRP

Synonyms:
SRP

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Unknown

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

Traveler's diarrhea vaccine

Synonyms:
Traveler's diarrhea vaccine

Disease:
Enterotoxigenic E. coli (ETEC)

Specific Indication:
Preventive, developed for use in travelers

Product Type:
Vaccine

PRV Elegible?
No

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:

Molecule Class:

Administration Route:
Transcutaneous

Notes:

Clinical Trials:

NCT00993681
NCT01040325
NCT00516659

Publications:

Developer Details

International Vaccine Institute (South Korea)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	Dukoral (ETEC)	Approved

Intercell AG (Austria)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	Traveler's diarrhea vaccine	Phase III

PATH (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	ACE527	Phase II

PATH (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	SBL 109	Phase I

PATH (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	LT/ST fusion proteins	Pre-clinical

PATH (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	dmLT	Phase I

PATH (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	Mimopath-based ETEC vaccine	Discovery

Tulane University (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	dmLT	Phase I

National Institute of Allergy and Infectious Diseases (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	Peru-15 pCTB (ETEC)	Phase I

National Institute of Allergy and Infectious Diseases (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	dmLT	Phase I

TD Vaccines A/S (Denmark)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	ACE527	Phase II

TD Vaccines A/S (Denmark)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	ACE920	Pre-clinical

Pierrel Research USA (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	ACE527	Phase II

Johns Hopkins Bloomberg School of Public Health (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	ACE527	Phase II

Crucell (Netherlands)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	SBL 109	Phase I

University of Colorado (United States)

Type	Disease	Product/Research Program	Current Phase

Vaccine	Enterotoxigenic E. coli (ETEC)	FTL-LTB chimera protein	Pre-clinical

Sanofi Pasteur (France)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	FTL-LTB chimera protein	Pre-clinical

Naval Medical Research Center (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	FTL-LTB chimera protein	Pre-clinical

International Enteric Vaccine Consortium (Norway)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	LT/ST fusion proteins	Pre-clinical

Research Council of Norway (Norway)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	LT/ST fusion proteins	Pre-clinical

University of Tennesee (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	EtpA glycoprotein	Pre-clinical

Syntiron (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	SRP	Discovery

Mucosal Immunobiology and Vaccine Center (Sweden)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	Mucosal immunobiology and vaccines discovery	Discovery

Mucosis B.V. (Netherlands)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Enterotoxigenic E. coli (ETEC)	Mimopath-based ETEC vaccine	Discovery