

Biopharmaceutical Researchers Testing 100 Medicines and Vaccines for HIV Infection and Related Conditions

HIV/AIDS is one of the most devastating diseases affecting people around the world. In 2008, an estimated 33.4 million people worldwide were living with HIV, 2.7 million new people were infected with HIV, and 2 million died from the disease, according to the Joint United Nation's Programme on HIV/AIDS (UNAIDS). The U.S. Centers for Disease Control and Prevention (CDC) estimates that more than 1 million Americans were living with HIV infection and nearly 600,000 died from the disease at the end of 2007.

To help fight this global epidemic, biopharmaceutical researchers are testing 100 medicines to treat HIV/AIDS and related conditions and intensifying their efforts to develop preventative vaccines. Since first identifying the HIV virus in 1983, 31 medicines have been approved to treat HIV infection. These approved medicines have helped to prolong the lives of HIV-infected patients. According to the CDC, deaths from AIDS decreased in the United States by 17 percent from 2003 through 2007.

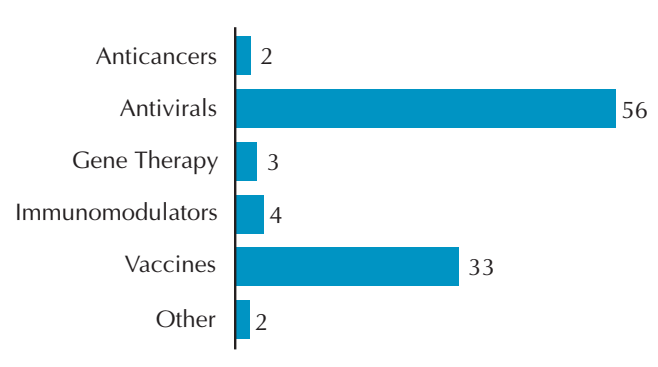
But treatment alone is not enough to combat HIV/AIDS. For every two patients who begin receiving HIV treatment, five people become infected. A preventative vaccine is crucial to the fight against AIDS. "A safe and effective HIV vaccine is critical to the control of HIV globally," says Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID). According to the International AIDS Vaccine Initiative (IAVI), without a significant improvement in prevention efforts, including an HIV vaccine, infections could double from about 5 million a year in 2005 to 10 million a year by 2030. IAVI estimates that the potential positive impact of AIDS vaccines would be enormous, especially in the developing world.

Conservatively, a vaccine that is 50 percent effective and given to only 30 percent of the population could reduce new HIV infections by 34 percent over 15 years, according to IAVI. Currently, 33 vaccines are in development.

In addition to the vaccines, there are 56 antivirals, two cancer treatments, four immunomodulators, three gene therapies, and two other medicines now in human clinical trials or before the Food and Drug Administration awaiting approval.

Examples of HIV medicines and vaccines in the pipeline include:

MEDICINES IN DEVELOPMENT FOR AIDS



- An antisense gene therapy that uses genetic material derived from HIV-1 itself to remove disease-causing aspects of the virus.
- A transdermal vaccine comprised of DNA plasmids that helps suppress virus replication and destroys HIV-infected cells.
- One in a new class of medicines is intended to prevent the HIV virus from attaching to new cells and breaking through the cell membrane.

Opportunistic infections are a particular problem for patients infected with the HIV virus. These infections include candidiasis of the mouth (thrush), the most common opportunistic infection in people with HIV; *Mycobacterium avium* complex (MAC), a bacterial infection that up to 50 percent of people with AIDS may develop; and *Pneumocystis carinii* pneumonia (PCP), the most common AIDS-defining infection in the United States. A separate PhRMA report on *Medicines in Development for Infectious Diseases* contains information on medicines in the pipeline for HIV-related opportunistic infections. The report can be found at www.phrma.org.

While HIV/AIDS remains a formidable foe and worldwide scourge, America's biopharmaceutical research companies are continuing their efforts to develop novel and more effective therapies and vaccines to contain the disease and improve and lengthen the lives of patients.

John J. Castellani
 President and CEO
 PhRMA

Medicines in Development for HIV/AIDS

ANTICANCERS

Product Name	Sponsor	Indication	Development Status*
PTC299	PTC Therapeutics <i>South Plainfield, NJ</i>	Kaposi's sarcoma	Phase I/II (908) 222-7000
veglin	VasGene Therapeutics <i>Los Angeles, CA</i>	Kaposi's sarcoma	Phase I (323) 221-7818

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
Alferon LDO [®] interferon-alpha-n3	Hemispherx Biopharma <i>Philadelphia, PA</i>	HIV infection treatment	Phase II (215) 988-0080
AMD-070 (CXCR4 receptor antagonist)	Genzyme <i>Cambridge, MA</i> National Institute of Allergy and Infectious Diseases (NIAID) <i>Bethesda, MD</i>	HIV-1 infection treatment	Phase I/II completed (617) 252-7500
amdoxovir (DAPD)	RFS Pharma <i>Tucker, GA</i>	HIV-1 infection treatment (combination therapy)	Phase II completed (404) 601-1430
Ampligen [®] rintatolimod	Hemispherx Biopharma <i>Philadelphia, PA</i>	HIV infection treatment	Phase II (215) 988-0080
anti-HIV-1 mAb combination (2G12,2F5,4E10)	Polymun Scientific <i>Vienna, Austria</i>	HIV infection treatment	Phase II completed www.polymun.com
ATI-0312	Arisyn Therapeutics <i>Frederick, MD</i>	HIV infection treatment	Phase I (301) 644-3921
ATI-0917	Arisyn Therapeutics <i>Frederick, MD</i>	HIV infection	Phase I (301) 644-3921
CB1922 (synthetic steroidal lactone)	Canopus BioPharma <i>Studio City, CA</i>	HIV infection	Phase II www.canopusbiopharma.com
CMX157 (tenofovir PIM conjugate)	Chimerix <i>Durham, NC</i>	HIV infection	Phase I (919) 806-1074
cobicistat (pk coenhancer)	Gilead Sciences <i>Foster City, CA</i>	HIV infection	Phase III (650) 574-3000
CTP-518 (PI)	Concert Pharmaceuticals <i>Lexington, MA</i> GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	HIV infection	Phase I (781) 860-0045 (888) 825-5249
Cytolin [®] anti-CD8 mAb	CytoDyn <i>Sante Fe, NM</i>	HIV infection	Phase I (505) 988-5520

* For more information about a specific medicine in this report, please use contact information provided.

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
dapivirine vaginal gel (NNRTI)	International Partnership for Microbicides <i>Silver Spring, MD</i>	prevention of HIV transmission in women	Phase I/II (301) 608-2221
darunavir/TMC41629	Tibotec Pharmaceuticals <i>County Cork, Ireland</i> Tibotec Therapeutics <i>Titusville, NJ</i>	HIV infection	Phase I completed (609) 730-6000
efavirenz/lamivudine/tenofovir fumarate fixed-dose combination	Matrix Laboratories <i>Secunderabad, India</i> Mylan <i>Canonsburg, PA</i>	HIV-1 infection	application submitted (724) 514-1800
elvitegravir (integrase inhibitor)	Gilead Sciences <i>Foster City, CA</i>	HIV-1 infection treatment	Phase III (650) 574-3000
elvitegravir/emtricitabine/tenofovir disoproxil fumarate/cobicistat fixed-dose combination	Gilead Sciences <i>Foster City, CA</i>	HIV infection treatment (in treatment-naive patients)	Phase III (650) 574-3000
elvucitabine (NRTI)	Achillion Pharmaceuticals <i>New Haven, CT</i>	HIV infection (combination therapy in treatment-naive patients)	Phase II (203) 624-7000
		HIV infection (in treatment-experienced patients)	Phase II (203) 624-7000
emtricitabine/tenofovir fumarate/rilpivirine (TMC278) fixed-dose combination (NNRTI)	Gilead Sciences <i>Foster City, CA</i> Tibotec Pharmaceuticals <i>County Cork, Ireland</i>	HIV-1 infection (in treatment-naive patients)	Phase III (650) 574-3000
Festinavir [®] (OBP601) (NRTI)	Oncolys BioPharma <i>Tokyo, Japan</i>	HIV-1 infection	Phase II www.oncolys.com
GS 7340 (nucleotide)	Gilead Sciences <i>Foster City, CA</i>	HIV infection	Phase I (650) 574-3000
GSK1247303 (S-247303) (integrase inhibitor)	Shionogi <i>Florham Park, NJ</i> ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV-1 infection	Phase II (973) 966-6900 (877) 844-8872
GSK1265744 (S-265744) (integrase inhibitor)	Shionogi <i>Florham Park, NJ</i> ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment	Phase II completed (973) 966-6900 (877) 844-8872

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
GSK1349572 (S-349572) (integrase inhibitor)	Shionogi <i>Florham Park, NJ</i> ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment	Phase II (973) 966-6900 (877) 844-8872
GSK2248761 (IDX-899) (NNRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV-1 infection treatment	Phase II (877) 844-8872
HIV attachment inhibitor	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection	in clinical trials (212) 546-4000
Intellece™ etravirine (NNRTI)	Tibotec Pharmaceuticals <i>County Cork, Ireland</i> Tibotec Therapeutics <i>Titusville, NJ</i>	HIV infection combination therapy in treatment-naive patients (Fast Track)	Phase II (609) 730-6000
		HIV-1 infection in adolescents, children, treatment-experienced patients (combination therapy)	Phase II (609) 730-6000
Isentress® raltegravir (integrase inhibitor)	Merck <i>Whitehouse Station, NJ</i>	HIV-1 infection in adolescents, children, treatment-experienced patients	Phase I/II (800) 672-6372
Kaletra® lopinavir/ritonavir (PI)	Abbott Laboratories <i>Abbott Park, IL</i>	HIV infection (combination therapy)	Phase III (847) 937-6100
KD-247 (monoclonal antibody)	Katetsuken <i>Kumamoto, Japan</i>	HIV-1 infection	Phase I
KP-1461 (HIV replication inhibitor)	Koronis Pharmaceuticals <i>Redmond, WA</i>	HIV infection therapy in treatment-experienced patients	Phase II (425) 825-0240
Lexiva® fosamprenavir calcium (PI)	Vertex Pharmaceuticals <i>Cambridge, MA</i> ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection in adolescents and children	Phase II (617) 444-6100 (877) 844-8872
MK-4965 (NNRTI)	Merck <i>Whitehouse Station, NJ</i>	HIV-1 infection treatment	Phase I (800) 672-6372
PF-232798 (CCR5 receptor antagonist)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment	Phase II (877) 844-8872
PF-4776548	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection	Phase I (877) 844-8872
PRO-140 (CCR5 receptor antagonist)	Progenics Pharmaceuticals <i>Tarrytown, NY</i>	HIV-1 infection (Fast Track)	Phase II (914) 789-2800
Racivir® PSI-5004 (NRTI)	Pharmasset <i>Princeton, NJ</i>	HIV infection treatment	Phase II completed (609) 613-4100
RDEA427 (NNRTI)	Ardea Biosciences <i>San Diego, CA</i>	HIV infection	Phase 0 completed (858) 652-6500

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
RDEA806 (NNRTI)	Ardea Biosciences <i>San Diego, CA</i>	HIV infection	Phase II completed (858) 652-6500
Reyataz™ atazanavir (PI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection (pediatric)	in clinical trials (212) 546-4000
rilpivirine (TMC278) (NNRTI)	Tibotec Pharmaceuticals <i>County Cork, Ireland</i> Tibotec Therapeutics <i>Titusville, NJ</i>	HIV-1 infection therapy in treatment-naïve patients	application submitted (609) 730-6000
RPI-MN	ReceptoPharm <i>Plantation, FL</i>	HIV infection	Phase II (954) 321-8988
SCH-532706 (CCR5 receptor antagonist)	Merck <i>Whitehouse Station, NJ</i>	HIV infection treatment	Phase I (800) 672-6372
SP-01A (procaine oral)	Pharmaplaz <i>Co. Roscommon, Ireland</i> Samaritan Pharmaceuticals <i>Las Vegas, NV</i>	HIV infection treatment in patients failing triple HIV therapy (monotherapy)	Phase II/III (702) 735-7001
SPL-7013	Starpharma <i>Melbourne, Australia</i>	HIV infection prevention (Fast Track)	Phase I completed www.starpharma.com
Sustiva™ efavirenz (NNRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection (pediatric)	in clinical trials (212) 546-4000
Tarvacin™ bavituximab	Peregrine Pharmaceuticals <i>Tustin, CA</i>	HIV co-infection with hepatitis C	Phase I (714) 508-6000
TBR-220 (CCR5 receptor antagonist)	Tobira Therapeutics <i>Princeton, NJ</i>	HIV-1 infection treatment	Phase I (781) 635-4346
TBR-652 (CCR5 receptor antagonist)	Tobira Therapeutics <i>Princeton, NJ</i>	HIV-1 infection treatment	Phase II (781) 635-4346
tenofovir vaginal gel (NRTI)	CONRAD <i>Arlington, VA</i> Gilead Sciences <i>Foster City, CA</i> International Partnership for Microbicides <i>Silver Spring, MD</i>	HIV infection (Fast Track)	Phase II (703) 524-4744 (301) 608-2221
TMC310911 (PI)	Tibotec Pharmaceuticals <i>County Cork, Ireland</i> Tibotec Therapeutics <i>Titusville, NJ</i>	HIV infection treatment	Phase I/II (609) 730-6000
TRI-1144 (fusion inhibitor)	Trimeris <i>Durham, NC</i>	HIV infection treatment	Phase I (919) 806-4682
UB-421	United Biomedical <i>Hauppauge, NY</i>	HIV-1 infection in treatment-naïve patients	Phase I (631) 273-2828
UC-781 vaginal gel (NNRTI)	CONRAD <i>Arlington, VA</i>	HIV infection prevention	Phase I (703) 524-4744

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
UK-453061 (NNRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment	Phase II (877) 844-8872
VRX806 (NNRTI)	Valeant Pharmaceuticals <i>Mississauga, Canada</i>	HIV infection treatment	Phase II (905) 286-3000

GENE THERAPY

Product Name	Sponsor	Indication	Development Status
lexgenleucel-T (HIV replication inhibitor)	VIRxSYS <i>Gaithersburg, MD</i>	HIV infection therapy in treatment-experienced patients	Phase II (301) 987-0480
SB-728-T	Sangamo BioSciences <i>Richmond, CA</i>	HIV infection	Phase I/II (510) 970-6000
StealthVector [®] HGTV-43 [™] antisense gene medicine	Enzo Therapeutics <i>New York, NY</i>	HIV-1 infection treatment	Phase I/II (212) 583-0100

IMMUNOMODULATORS

Product Name	Sponsor	Indication	Development Status
AMZ0026	Amazon Biotech <i>New York, NY</i>	HIV infection treatment	Phase II (212) 444-1019
CYT107 (recombinant human interleukin-7)	Cytheris <i>Rockville, MD</i>	HIV infection treatment	Phase II (301) 231-0450
OHR/AVR118	Ohr Pharmaceuticals <i>New York, NY</i>	AIDS-related cachexia	Phase II (212) 682-8452
TXA127	Tarix Pharmaceuticals <i>Brookline, MA</i>	low T-lymphocyte counts in patients with HIV infection	Phase I (617) 827-6824

VACCINES

Product Name	Sponsor	Indication	Development Status
Ad5.ENVA.48 HIV-1 vaccine	National Institute of Allergy and Infectious Diseases <i>Bethesda, MD</i>	HIV-1 infection prevention	Phase I www.niaid.nih.gov
Ad26.ENVA.01 HIV-1 recombinant vaccine	Crucell <i>Leiden, The Netherlands</i> Beth Israel Deaconess Medical Center <i>Boston, MA</i> International AIDS Vaccine Initiative <i>New York, NY</i>	HIV infection prevention	Phase I (212) 847-1111

VACCINES

Product Name	Sponsor	Indication	Development Status
Ad35-ENV vaccine	Beth Israel Deaconess Medical Center <i>Boston, MA</i> International AIDS Vaccine Initiative <i>New York, NY</i>	HIV infection prevention	Phase I (212) 847-1111
Ad35-GRIN/ENV vaccine	International AIDS Vaccine Initiative <i>New York, NY</i> University of Rochester Medical Center <i>Rochester, NY</i>	HIV infection prevention	Phase I (212) 847-1111
ADVAX (DNA vaccine)	Aaron Diamond AIDS Research Center <i>New York, NY</i> International AIDS Vaccine Initiative <i>New York, NY</i> Ichor Medical Systems <i>San Diego, CA</i>	HIV infection prevention ----- HIV infection prevention (new delivery system)	Phase I (212) 448-5000 (212) 847-1111 Phase I (212) 448-5000 (212) 847-1111
AGS-004 (autologous dendritic cell vaccine)	Argos Therapeutics <i>Durham, NC</i>	HIV-1 infection treatment	Phase II (919) 287-6300
AVX101 (single gene HIV vaccine)	AlphaVax <i>Rsch. Triangle Park, NC</i>	HIV-1 infection	Phase I completed (919) 595-0400
CDX-2401 (antigen presenting cell-targeting vaccine)	Celldex Therapeutics <i>Needham, MA</i> Rockefeller University <i>New York, NY</i>	HIV infection	Phase I (781) 433-0771
DermaVir™ DNA topical vaccine	Genetic Immunity <i>McLean, VA</i>	HIV-1 infection treatment	Phase II (703) 879-6803
EP1043 (recombinant protein vaccine)	VaxOnco <i>Seoul, South Korea</i> National Institute of Allergy and Infectious Diseases <i>Bethesda, MD</i>	HIV-1 infection prevention	Phase I completed www.vaxonco.com
EP1090 (DNA vaccine)	VaxOnco <i>Seoul, South Korea</i> National Institute of Allergy and Infectious Diseases <i>Bethesda, MD</i>	HIV-1 infection prevention and treatment	Phase I/II www.vaxonco.com
HIV recombinant vaccine	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	HIV infection prevention	Phase II (888) 825-5249

VACCINES

Product Name	Sponsor	Indication	Development Status
HIV vaccine	GeoVax Labs <i>Smyrna, GA</i>	HIV-1 infection prevention	Phase II (678) 384-7220
HIV vaccine	GeoVax Labs <i>Smyrna, GA</i>	HIV-1 infection treatment	Phase I (678) 384-7220
HIV vaccine	Massachusetts General Hospital <i>Boston, MA</i> Opal Therapeutics <i>Parkvill, Australia</i>	HIV infection	Phase I (617) 726-2000
HIV vaccine	Novartis Vaccines <i>Cambridge, MA</i>	HIV infection	Phase I (888) 669-6682
HIV vaccine	sanofi pasteur <i>Swiftwater, PA</i>	HIV infection prevention	Phase III (570) 839-4267
MVA-BN® HIV multiantigen vaccine	Bavarian Nordic <i>Washington, DC</i>	HIV-1 infection prevention and treatment	Phase I/II (202) 536-1581
NYVAC-B	EuroVacc <i>Amsterdam, The Netherlands</i> HIV Vaccine Trials Network <i>Seattle, WA</i> National Institute of Allergy and Infectious Diseases <i>Bethesda, MD</i>	HIV infection prevention	Phase I (800) 448-0440 www.niaid.nih.gov
Pennvax™-B DNA vaccine (clade B)	Inovio Pharmaceuticals <i>Blue Bell, PA</i>	HIV infection prevention and treatment	Phase I (267) 440-4200
Pennvax™-G DNA vaccine (clades A, C, D)	Inovio Pharmaceuticals <i>Blue Bell, PA</i>	HIV infection prevention	Phase I (267) 440-4200
SAAVI DNA-C2 vaccine	HIV Vaccine Trials Network <i>Seattle, WA</i> National Institute of Allergy and Infectious Diseases <i>Bethesda, MD</i>	HIV infection prevention	Phase I (800) 448-0440 www.niaid.nih.gov
SAAVI MVA-C vaccine	HIV Vaccine Trials Network <i>Seattle, WA</i> National Institute of Allergy and Infectious Diseases <i>Bethesda, MD</i>	HIV infection prevention	Phase I (800) 448-0440 www.niaid.nih.gov
TBC-M4 (MVA HIV vaccine)	Aaron Diamond AIDS Research Center <i>New York, NY</i> International AIDS Vaccine Initiative <i>New York, NY</i>	HIV infection prevention	Phase I (212) 448-5000 (212) 847-1111
tgAAC09	Targeted Genetics <i>Seattle, WA</i>	HIV infection prevention	Phase II completed (206) 623-7612

VACCINES

Product Name	Sponsor	Indication	Development Status
TUTI-16	Thymon <i>Short Hills, NJ</i>	HIV-1 infection	Phase I/II (973) 467-9558
V526	Merck <i>Whitehouse Station, NJ</i>	HIV infection prevention	Phase I (800) 672-6372
vacc-4x	Bionor Pharma <i>Bethesda, MD</i>	HIV-1 infection treatment	Phase II (301) 571-9493
VRC-HIVADV 014-00-VP (HIV-1 recombinant adenovirus vaccine)	GenVec <i>Gaithersburg, MD</i> Vaccine Research Center (NIAID) <i>Bethesda, MD</i>	HIV infection prevention	Phase II (240) 632-0740 www.vrc.nih.gov
VRC-HIVADV- 027-00-VP (HIV adenovector Ad35 vaccine)	GenVec <i>Gaithersburg, MD</i> Vaccine Research Center (NIAID) <i>Bethesda, MD</i>	HIV infection prevention	Phase I (240) 632-0740 www.vrc.nih.gov
VRC-HIVADV 038-00-VP (HIV adenovector Ad5 vaccine)	Vaccine Research Center (NIAID) <i>Bethesda, MD</i>	HIV infection prevention	Phase I www.vrc.nih.gov
VRC-HIVDNA 016-00-VP (DNA plasmid vaccine)	Vaccine Research Center (NIAID) <i>Bethesda, MD</i>	HIV infection prevention	Phase II www.vrc.nih.gov
VRC-HIVDNA 044-00-VP (HIV DNA vaccine)	Vaccine Research Center (NIAID) <i>Bethesda, MD</i>	HIV infection prevention	Phase I www.vrc.nih.gov

OTHER

Product Name	Sponsor	Indication	Development Status
ibalizumab (TMB-355)	TaiMed Biologies USA <i>Irvine, CA</i>	HIV infection treatment (Fast Track)	Phase II completed (949) 769-6543
Lyrica [®] pregabalin	Pfizer <i>New York, NY</i>	HIV-associated neuropathy	Phase III (860) 732-5156

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
Agenerase [®] amprenavir (PI)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i> Vertex Pharmaceuticals <i>Cambridge, MA</i>	treatment of HIV infection in combination with other antiviral medications
Aptivus [®] tipranavir (PI)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	advanced HIV-1 infection in combination with other medications; pediatric and adolescent treatment-experienced patients

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
Atripla [®] efavirenz/ emtricitabine/ tenofovir disoproxil fumarate (fixed-dose combination tablet) (NNRTI/NRTI/NtRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i> Gilead Sciences <i>Foster City, CA</i>	treatment of HIV-1 infection in adults
Combivir [®] lamivudine/ zidovudine tablets (NRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment
Crixivan [®] indinavir sulfate (PI)	Merck <i>Whitehouse Station, NJ</i>	HIV infection treatment
Emtriva [®] emtricitabine (NRTI)	Gilead Sciences <i>Foster City, CA</i>	HIV infection in combination with other antiretroviral medications
Epivir [®] lamivudine (NRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment, HIV infection (once-daily dosing)
Epzicom [™] lamivudine and abacavir sulfate (once-daily) (NRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection in combination with other antiretroviral medications
Fuzeon [®] enfuvirtide (FI)	Roche <i>Nutley, NJ</i> Trimeris <i>Durham, NC</i>	in combination with other antiretroviral agents for HIV infection
Hivid [®] zalcitabine (NRTI)	Roche <i>Nutley, NJ</i>	in combination with other antiviral agents for treatment of HIV infection
Insectress [®] raltegravir (integrase inhibitor)	Merck <i>Whitehouse Station, NJ</i>	in combination with other antiretroviral agents for the treatment of HIV infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents
Intelence [™] etravirine (NNRTI)	Tibotec Therapeutics <i>Bridgewater, NJ</i>	treatment of HIV-1 infection in treatment-experienced patients
Invirase [®] saquinavir mesylate (PI)	Roche <i>Nutley, NJ</i>	treatment of HIV infection in combination with other antiviral agents
Kaletra [®] lopinavir/ritonavir (PI)	Abbott Laboratories <i>Abbott Park, IL</i>	treatment of HIV infection in adults and children; treatment of HIV infection (new dosing [PI] regimen)

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
Lexiva [®] fosamprenavir calcium (PI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i> Vertex Pharmaceuticals <i>Cambridge, MA</i>	treatment of HIV infection in combination with other antiretroviral medications
Norvir [®] ritonavir (PI)	Abbott Laboratories <i>Abbott Park, IL</i>	HIV infection (pediatric and adult)
Prezista [®] darunavir (PI)	Tibotec Therapeutics <i>Bridgewater, NJ</i>	treatment of HIV infection in antiretroviral treatment-experienced adult patients; pediatric patients 6 years and older
Rescriptor [®] delvaridine (NNRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	treatment of HIV infection as part of a combination therapy regimen
Retrovir [®] zidovudine (NRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV positive (asymptomatic [CD4<500] and symptomatic [ARC, AIDS]), pediatric and adult, prevention of maternal/fetal transmission of HIV infection
Reyataz [®] atazanavir (PI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	treatment of HIV-1 infection in combination with other antiretroviral medications; boost treatment-naive HIV-1 infection treatment
Selzentry [®] maraviroc (CCR5 antagonist)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	combination antiretroviral treatment of adults infected with only CCR5-tropic HIV detectable who have evidence of viral replication and have HIV strains resistant to multiple antiretroviral agents
Sustiva [®] efavirenz (NNRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection, HIV infection (once-daily)
Trizivir [®] abacavir, lamivudine and zidovudine combination tablet (NRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection treatment
Truvada [®] emtricitabine/ tenofovir disoproxil fumarate (NRTI)	Gilead Sciences <i>Foster City, CA</i>	HIV infection in combination with other antiretroviral agents
Videx [®] didanosine (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection, once-daily dosing, pediatric HIV infection
Videx [®] EC didanosine, enteric coated (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection
Viracept [®] nelfinavir mesylate (PI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	HIV infection/AIDS (pediatric and adult)

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
Viramune [®] nevirapine (NNRTI)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	for use in combination with other antiretroviral agents for the treatment of HIV-1 infection
Viread [®] tenofovir disoproxil fumarate (NtRTI)	Gilead Sciences <i>Foster City, CA</i>	HIV infection in combination with other antiretroviral agents
Zerit [®] stavudine (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection, pediatric HIV infection, first-line in combination treatment
Ziagen [®] abacavir (NRTI)	ViiV Healthcare <i>Rsch. Triangle Park, NC</i>	treatment of HIV infection in combination with other antiretroviral medications

The content of this report has been obtained through industry sources and the Adis “R&D Insight” database based on the latest information. **Report current as of November 17, 2010.** The information may not be comprehensive. For more specific information about a particular product, contact the individual company directly or go to www.clinicaltrials.gov. The entire series of *Medicines in Development* is available on PhRMA’s web site.

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GLOSSARY

application submitted—Application for marketing has been submitted to the Food and Drug Administration (FDA).

cachexia—A wasting syndrome that causes weakness and a loss of weight, fat, and muscle. Anorexia (lack of appetite) and cachexia often occur together. Cachexia can occur in people who are eating enough, but who cannot absorb the nutrients. Cachexia is not the same as starvation. A healthy person's body can adjust to starvation by slowing down its use of nutrients, but in cachectic patients, the body does not make that adjustment. Patients with advanced cancer, AIDS, and some other major chronic progressive diseases may appear cachectic.

FI—Fusion inhibitor.

HIV infection—Presence of antibodies in the blood to the human immunodeficiency virus (the virus that causes AIDS). **HIV-1** refers to the most common strain of the virus found in U.S. AIDS patients.

Kaposi's sarcoma—A rare malignant skin tumor that occurs in some AIDS patients. It can be accompanied by fever, enlarged lymph nodes and gastrointestinal problems.

lipodystrophy—A group of rare metabolic disorders which can be either inherited or acquired. They are characterized by abnormalities in fatty (adipose) tissue associated with total or partial loss of body fat, abnormalities of carbohydrate and lipid metabolism, severe resistance to naturally occurring and synthetic insulin, and immune system dysfunction. These disorders are differentiated by degrees of severity, and by areas or systems of the body affected. Lipodystrophies can also be associated with other disorders and various developmental abnormalities.

neuropathy—Caused by disease, inflammation, or damage to the peripheral nerves, which connect the central nervous system (brain and spinal cord) to the sense organs, muscles, glands, and internal organs.

NRTI—Nucleoside reverse transcriptase inhibitor.

NNRTI—Non-nucleoside reverse transcriptase inhibitor.

NtRTI—Nucleotide analogue reverse transcriptase inhibitor.

Phase 0—First-in-human trials conducted in accordance with FDA's 2006 guidance on exploratory Investigational New Drug (IND) studies designed to speed up development of promising drugs by establishing very early on whether the agent behaves in human subjects as was anticipated from preclinical studies.

Phase I—Safety testing and pharmacological profiling in humans.

Phase II—Effectiveness and safety testing in humans.

Phase III—Extensive clinical trials to demonstrate safety and efficacy in humans.

PI—Protease inhibitor.

SELECTED FACTS ABOUT HIV/AIDS

	U.S. AIDS Cases through 2008 ¹	U.S. AIDS Deaths through 2007 ¹
Adults/Adolescents	1,063,778	571,453
Pediatric (under age 13)	9,349	4,931
TOTAL	1,106,391*	597,499*

HIV/AIDS Worldwide²

- The number of people living with HIV worldwide continued to grow in 2008, reaching an estimated 33.4 million. The total number of people living with the virus in 2008 was more than 20 percent higher than the number in 2000, and the prevalence was roughly threefold higher than in 1990.
- The continuing rise in the population of people living with HIV reflects the combined effects of continued high rates of new HIV infections and the beneficial impact of antiretroviral therapy. As of December 2008, approximately 4 million people in low- and middle-income countries were receiving antiretroviral therapy—a 10-fold increase over five years.
- Worldwide in 2008, an estimated 2.7 million new HIV infections occurred, and some 2 million deaths resulted due to AIDS-related illnesses. The latest data indicate that globally the spread of HIV appears to have peaked in 1996, when 3.5 million new HIV infections occurred. In 2008, the estimated number of new HIV infections was approximately 30 percent lower than at the epidemic's peak 12 years earlier.
- Annual HIV-related mortality appears to have peaked in 2004, when 2.2 million deaths occurred. The estimated number of AIDS-related deaths in 2008 is roughly 10 percent lower than in 2004.
- Sub-Saharan Africa remains the region most heavily affected by HIV. In 2008, sub-Saharan Africa accounted for 67 percent of HIV infections worldwide, 68 percent of new HIV infections among adults, and 91 percent of new HIV infections among children. The region also accounted for 72 percent of the world's AIDS-related deaths in 2008, when more than 14.1 million children in sub-Saharan Africa were estimated to have lost one or both parents to AIDS.
- Women and girls continue to be affected disproportionately by HIV in sub-Saharan Africa. For example, in Côte d'Ivoire, home to the most serious epidemic in West Africa, HIV prevalence among females (6.4 percent) was more than twice as high as among males (2.9 percent) in 2005. In sub-Saharan Africa as a whole, women account for approximately 60 percent of estimated HIV infections.
- Across the globe, an estimated 430,000 new HIV infections occurred among children under the age of 15 in 2008. Most of these new infections are believed to stem from transmission during childbirth or post-partum as a result of breastfeeding. The number of children newly infected with HIV in 2008 was roughly 18 percent lower than in 2001.
- Globally, coverage for services to prevent mother-to-child HIV transmission rose from 10 percent in 2004 to 45 percent in 2008, and the drop in new HIV infections among children that year suggests that these efforts are saving lives.

HIV/AIDS in the United States¹

- In 2008, the Centers for Disease Control and Prevention (CDC) estimated that approximately 56,300 people were newly infected with HIV in 2006 (the most recent year that data are available). More than half (53 percent) of those new infections occurred in gay and bisexual men. Black/African-American men and women were also strongly affected and were estimated to have an incidence rate that was seven times as high as the incidence rate among whites.

* Cumulative totals include people of unknown race/ethnicity. Because totals for the estimated numbers were calculated independently of the values for the subpopulations, the subpopulation values may not equal the totals.¹

SELECTED FACTS ABOUT HIV/AIDS

HIV/AIDS in the United States¹ (continued)

- At the end of 2007, the estimated number of people living with a diagnosis of HIV infection (*in the 37 states and five U.S. dependent areas with confidential name-based HIV infection reporting*) was 599,819. In the 37 states only, that total included 577,452 adults and adolescents, and 2,919 children under the age of 13. (*Data include people with a diagnosis of HIV infection regardless of the stage of disease at diagnosis.*)
 - In 2008, the estimated number of people diagnosed with AIDS in the United States and dependent areas was 37,991. Of these, 37,151 were diagnosed in the 50 states and the District of Columbia and 840 were diagnosed in the dependent areas. In the 50 states and the District of Columbia, 27,543 AIDS diagnoses were among adult and adolescent males, 9,567 were among adult and adolescent females, and 41 diagnoses were among children under the age of 13.
 - In 2008, the cumulative estimated number of AIDS diagnoses in the 50 states and the District of Columbia, by race or ethnicity was as follows:
 - American Indian/Alaska Native, 3,741
 - Asian, 8,253
 - Black/African American, 452,916
 - Hispanic/Latino, 180,061
 - Native Hawaiian/Pacific Islander, 830
 - White, 419,905
 - Multiple Races, 7,054
 - In 2007, the estimated number of deaths of people with an AIDS diagnosis in the United States and dependent areas was 18,089. In the 50 states and the District of Columbia, this included 17,613 adults and adolescents and six children under the age of 13.
 - The cumulative estimated number of deaths of people with an AIDS diagnosis in the United States and dependent areas, through 2007, was 597,499. In those areas, that total included 571,453 adults and adolescents and 4,931 children under the age of 13.
-

HIV-Related Conditions

- Before the AIDS epidemic, **Kaposi's sarcoma (KS)** rarely occurred in the United States. About two new cases of KS were found for every 1 million people in this country annually. Now, most KS cases occur in people infected with HIV. It has been estimated that an HIV-infected person has a 20,000-fold increased risk of developing KS compared with people who do not have HIV. AIDS patients with KS increased the rate of KS in this country more than 20 times, peaking at 47 cases per 1 million people annually in the early 1990s. With new treatments for AIDS, KS has become less common, with about six cases per million people each year. KS is much more common in men than in women, and it is rarely seen in children.³
 - The HIV-associated **lipodystrophy syndrome** (characterized by alterations in body appearance related to changes in body fat stores) has been described in up to 80 percent of patients who have been exposed to antiretroviral therapies. One study found that total healthcare expenditures were estimated to be \$1,718 more for HIV-infected subjects with lipodystrophy than for HIV-infected subjects without lipodystrophy.⁴
 - It is estimated that nearly one-third of people with HIV/AIDS experience some peripheral nerve damage. For patients with HIV/AIDS, peripheral **neuropathy** can be caused by the virus itself, by certain drugs used in the treatment of HIV/AIDS or other complications, or as a result of opportunistic infections (e.g., cytomegalovirus, candidiasis, tuberculosis).⁵
-

Economic Impact

- A recent study found that the total lifetime cost of illness for Americans newly diagnosed with **HIV** in 2002 is approximately \$36.4 billion, of which more than 80 percent is related to productivity losses.⁶

SELECTED FACTS ABOUT HIV/AIDS

Economic Impact (continued)

- Differences in medical care result in dissimilar costs—both direct and indirect—among different racial and ethnic groups. Minorities are, on average, diagnosed at later stages of the disease than whites, who are more likely to receive antiretroviral therapy (ART). Researchers found that patients on ART have direct medical costs averaging \$230,044, with a projected life expectancy of 24.4 years. Patients not receiving ART have direct medical costs of approximately \$114,938, with a projected life expectancy of 12.4 years. Minorities incur fewer direct medical costs than whites (\$160,400 for African Americans on average, compared with \$180,900 for whites), but suffer greater financial damage from lost productivity (\$838,000 for Hispanics and \$766,800 for African Americans on average, compared with \$661,100 for whites).⁶
- Without intervention, a perinatal **HIV** transmission rate of 25 percent would result in 1,750 HIV-infected infants born annually in the United States with lifetime medical costs estimated to be \$282 million. The cost of intervention (HIV counseling, testing, and zidovudine treatment) was estimated to be \$67.6 million. That intervention would prevent 656 pediatric HIV infections, saving \$105.6 million in medical care costs—a net cost-savings of \$38.1 million annually.⁷

Sources:

1. U.S. Centers for Disease Control and Prevention, www.cdc.gov
2. Joint United Nations Programme on HIV/AIDS, www.unaids.org
3. American Cancer Society, www.cancer.org
4. AIDS Research and Therapy, BioMed Central Ltd., www.aidsrestherapy.com
5. University of Chicago, Peripheral Neuropathy Center, www.peripheralneuropathycenter.uchicago.edu
6. Medical News Today, MediLexicon International Ltd, www.medicalnewstoday.com
7. KidSource OnLine, Inc., www.kidsource.com

THE DRUG DISCOVERY, DEVELOPMENT AND APPROVAL PROCESS

It takes 10-15 years on average for an experimental drug to travel from the lab to U.S. patients. Only five in 5,000 compounds that enter preclinical testing make it to human testing. One of these five tested in people is approved.

Discovery/ Preclinical Testing		Clinical Trials			FDA	Phase IV
		Phase I	Phase II	Phase III		
Years	6.5	1.5	2	3.5	1.5	
Test Population	Laboratory and animal studies	20 to 100 healthy volunteers	100 to 500 patient volunteers	1,000 to 5,000 patient volunteers	Review process/ approval	Additional post-marketing testing required by FDA
Purpose	Assess safety, biological activity and formulations	Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use		
Success Rate	5,000 compounds evaluated	5 enter trials			1 approved	

THE DRUG DEVELOPMENT AND APPROVAL PROCESS

The U.S. system of new drug approvals is perhaps the most rigorous in the world.

It takes 10-15 years, on average, for an experimental drug to travel from lab to U.S. patients, according to the Tufts Center for the Study of Drug Development, based on drugs approved from 1994 through 1998. Only five in 5,000 compounds that enter preclinical testing make it to human testing. And only one of those five is approved for sale.

On average, it costs a company more than \$1 billion to get one new medicine from the laboratory to U.S. patients, according to a 2007 study by the Tufts Center for the Study of Drug Development.

Once a new compound has been identified in the laboratory, medicines are developed as follows:

Preclinical Testing. A pharmaceutical company conducts laboratory and animal studies to show biological activity of the compound against the targeted disease, and the compound is evaluated for safety.

Investigational New Drug Application (IND). After completing preclinical testing, a company files an IND with the U.S. Food and Drug Administration (FDA) to begin to test the drug in people. The IND shows results of previous experiments; how, where and by whom the new studies will be conducted; the chemical structure of the compound; how it is thought to work in the body; any toxic effects found in the animal studies; and how the compound is manufactured. All clinical trials must be reviewed and approved by the Institutional Review Board (IRB) where the trials will be conducted. Progress reports on clinical trials must be submitted at least annually to FDA and the IRB.

Clinical Trials, Phase I. These tests usually involve about 20 to 100 normal, healthy volunteers. The tests

study a drug's safety profile, including the safe dosage range. The studies also determine how a drug is absorbed, distributed, metabolized, and excreted as well as the duration of its action.

Clinical Trials, Phase II. In this phase, controlled trials of approximately 100 to 500 volunteer patients (people with the disease) assess a drug's effectiveness and determine the early side effect profile.

Clinical Trials, Phase III. This phase usually involves 1,000 to 5,000 patients in clinics and hospitals. Physicians monitor patients closely to confirm efficacy and identify adverse events.

New Drug Application (NDA)/Biologic License Application (BLA). Following the completion of all three phases of clinical trials, a company analyzes all of the data and files an NDA or BLA with FDA if the data successfully demonstrate both safety and effectiveness. The applications contain all of the scientific information that the company has gathered. Applications typically run 100,000 pages or more. The average review time for the 25 new therapeutics approved by the FDA in 2009 was 13.3 months.

Approval. Once FDA approves an NDA or BLA, the new medicine becomes available for physicians to prescribe. A company must continue to submit periodic reports to FDA, including any cases of adverse reactions and appropriate quality-control records. For some medicines, FDA requires additional trials (Phase IV) to evaluate long-term effects.

Discovering and developing safe and effective new medicines is a long, difficult, and expensive process. Pharmaceutical companies invested an estimated \$65.3 billion in research and development in 2009.

TRACKING THE BIOPHARMACEUTICAL RESEARCH PIPELINE

Today, more than 2,900 new medicines are in development in the United States. Many of these potential new medicines will fail in clinical trials, but some may represent tomorrow's new treatments. Bringing each new medicine to patients will require, on average, 10 to 15 years of testing and review.

PhRMA publishes several reports that track the biopharmaceutical research pipeline for many diseases, including the leading causes of death among Americans—heart disease, cancer, and stroke. The reports include medicines currently in clinical trials or at the U.S. Food and Drug Administration (FDA) for review. Below is a summary of our most popular reports.

- **Cancer**—There are few things that cause patients more fear and uncertainty as a cancer diagnosis. Yet today—because of a steady stream of new and improved medicines and treatments—cancer can increasingly be managed and even beaten. *The 2009 report found 861 medicines in the pipeline.*
- **Heart Disease and Stroke**—Keeping up the momentum of drug discovery that has helped cut deaths from heart disease and stroke in half in the past three decades, biopharmaceutical companies are working on new medicines for these diseases. *The 2009 report found 312 medicines in the pipeline.*
- **Diabetes**—Approximately 4,110 people are diagnosed with diabetes every day. To help fight this disease, pharmaceutical and biotechnology researchers are working on new medicines to treat it and related conditions. *The 2010 report found 235 medicines in the pipeline.*
- **Mental Illnesses**—Pharmaceutical and biotechnology researchers are testing many new medicines to help the more than 450 million people worldwide who suffer from some form of mental illness. *The 2010 report found 313 medicines in the pipeline.*
- **Biotechnology**—Millions of people have already benefited from medicines and vaccines developed through biotechnology, and a new report offers hope that many more will benefit in the future. *The 2008 report found 633 medicines in the pipeline.*
- **Children**—Biopharmaceutical researchers are testing medicines to meet the special needs of children. These medicines offer hope that the significant improvements achieved in children's health over the past few decades will continue and even accelerate. *The 2010 report found 234 medicines in clinical trials.*
- **Infectious Diseases**—Throughout history, infectious diseases have taken a devastating toll on the lives and well-being of people around the world. Today, vaccines and antibiotics have proven to be effective treatments in many cases, but infectious diseases still pose a very serious threat to patients. Infectious diseases may never be eradicated. But, new knowledge, new technologies, and a huge commitment of resources by America's biopharmaceutical research companies and the government can help meet the continuing—and ever-changing—threat from infectious diseases. *The 2010 report found 395 medicines in clinical trials.*



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