

HIV/AIDS

PRESENTED BY AMERICA'S PHARMACEUTICAL RESEARCH COMPANIES

Pharmaceutical Researchers Are Testing 92 Medicines And Vaccines for HIV and Related Conditions

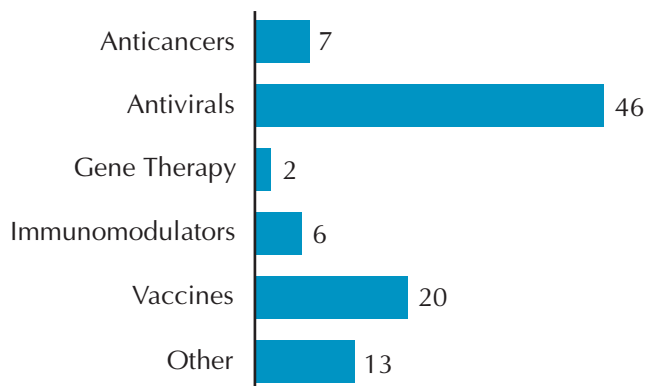
HIV/AIDS is one of the most devastating diseases affecting patients around the world. To help fight this global disease, pharmaceutical researchers are testing 92 medicines to treat HIV/AIDS and related conditions and intensifying their efforts to develop preventative vaccines. Since first identifying the AIDS virus in 1983, 30 medicines have been approved to treat HIV infection, including two in 2007.

According to the Joint United Nation's Programme on HIV/AIDS (UNAIDS), this year an estimated 33.2 million people worldwide were living with HIV, 2.5 million new people were infected with HIV, and 2.1 million died from the disease. The U.S. Centers for Disease Control and Prevention estimates that nearly 500,000 Americans were living with HIV infection at the end of 2005.

Preventative vaccine research is crucial to the continuing 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 around 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, an effective HIV vaccine could prevent almost 30 million of the 150 million new infections projected in the coming decades. A highly effective vaccine could even prevent more than 70 million infections in 15 years. Currently, 20 vaccines are in development.

In addition to the 20 vaccines now in development, there are 46 antivirals, seven cancer treatments, six immunomodulators, two gene therapies, and 13 other medicines now in human clinical trials or before the Food and Drug Administration awaiting approval.

Opportunistic infections are a particular problem for patients infected with the HIV virus. Opportunistic 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

MEDICINES IN DEVELOPMENT FOR AIDS*

*Some medicines are listed in more than one category.

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.

Examples of HIV medicines and vaccines in the pipeline include:

- A medicine that binds itself to a receptor protein found on the surface of human cells and blocks the HIV virus from entering the cell.
- An antisense gene therapy that uses two novel technologies to boost immune responsiveness against HIV.
- A vaccine that is designed to protect against the three most common types of HIV-1 virus found around the world.

While HIV/AIDS remains a formidable foe and worldwide scourge, America's pharmaceutical 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.

Billy Tauzin
President and CEO
PhRMA

Medicines in Development for HIV/AIDS

ANTICANCERS

Product Name	Sponsor	Indication	Development Status*
Multikine® leukocyte interleukin	Cel-Sci <i>Vienna, VA</i>	cervical dysplasia	Phase II (703) 506-9460
Myocet™ doxorubicin liposomal	Sopherion Therapeutics <i>Princeton, NJ</i>	Kaposi's sarcoma	in clinical trials (609) 986-2021
Panretin® Oral alitretinoin oral	Ligand Pharmaceuticals <i>San Diego, CA</i>	Kaposi's sarcoma	Phase II (858) 550-7500
Proleukin® aldesleukin	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	HIV-associated non-Hodgkin's lymphoma (see also immunomodulators)	Phase III (888) 669-6682
Targretin® Gel bexarotene topical	Ligand Pharmaceuticals <i>San Diego, CA</i>	Kaposi's sarcoma	Phase II (858) 550-7500
Thalomid® thalidomide	Celgene <i>Summit, NJ</i>	Kaposi's sarcoma (see also other)	Phase II (908) 673-9000
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>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	HIV infection treatment	Phase II (888) 253-3766
AMD-070	Genzyme <i>Cambridge, MA</i>	HIV-1 infection	Phase I (617) 252-7500
amdoxovir (NRTI)	RFS Pharma <i>Tucker, GA</i>	HIV infection treatment	Phase II (404) 601-1430
anti-HIV-1 mAb	Polymun Scientific <i>Vienna, Austria</i>	HIV infection treatment	Phase II www.polymun.com
apricitabine (NRTI)	Avexa <i>Richmond, Australia</i>	HIV-1 infection	Phase I www.avexa.com
BAY 50-4798	Bayer HealthCare Pharmaceuticals <i>West Haven, CT</i>	HIV infection treatment	Phase I/II (203) 812-2000
bevrimat (PA-457)	Panacos Pharmaceuticals <i>Watertown, MA</i>	HIV infection treatment	Phase II (617) 926-1551
BILR-355-BS (NNRTI)	Boehringer Ingelheim <i>Ridgefield, CT</i>	HIV infection	Phase II (800) 243-0127
C-2507	Merck <i>Whitehouse Station, NJ</i>	HIV infection	Phase I (800) 672-6372

* For more information about a specific medicine in this report, please call the telephone number listed.

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
calanolide A (NNRTI)	Sarawak MediChem Pharmaceuticals <i>Woodridge, IL</i>	HIV-1 infection	Phase I (630) 739-6744
dapivirine (TMC-120) (NNRTI)	International Partnership for Microbicides <i>Silver Spring, MD</i>	HIV infection prevention	Phase I (301) 608-2221
elvitegravir (GS-9137)	Gilead Sciences <i>Foster City, CA</i>	HIV infection treatment	Phase II (650) 574-3000
elvucitabine (Beta-L-Fd4C) (NRTI)	Achillion Pharmaceuticals <i>New Haven, CT</i> Vion Pharmaceuticals <i>New Haven, CT</i>	HIV infection treatment	Phase II (203) 624-7000
etravirine (TMC125) (NNRTI)	Tibotec Pharmaceuticals <i>Co. Cork, Ireland</i> <i>Yardley, PA</i>	HIV infection treatment	application submitted (609) 730-7500
fozivudine tidoxil (NRTI)	Heidelberg Pharma <i>Ladenburg, Germany</i>	HIV infection treatment	Phase II www.heidelberg-pharma.com
Fuzeon [®] enfuvirtide (fusion inhibitor)	Roche <i>Nutley, NJ</i> Trimeris <i>Morrisville, NC</i>	HIV-1 infection (once-daily dosing vs. twice-daily dosings)	Phase II (973) 235-5000 (919) 419-6050
GS-9131 (NRTI)	Gilead Sciences <i>Foster City, CA</i>	HIV-1 infection	Phase I (650) 574-3000
GS-9160 (integrase inhibitor)	Gilead Sciences <i>Foster City, CA</i>	HIV infection	Phase I (650) 574-3000
HGS-004 (CCR5-mAb)	Human Genome Sciences <i>Rockville, MD</i>	HIV infection treatment	Phase I (301) 309-8504
HIV attachment inhibitor	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection	Phase I (212) 546-4000
IDX-899 (NNRTI)	Idenix Pharmaceuticals <i>Cambridge, MA</i>	HIV-1 infection	Phase I (617) 995-9800
INCB 9471	Incyte <i>Wilmington, DE</i>	HIV infection treatment	Phase II (302) 498-6700
INCB 15050	Incyte <i>Wilmington, DE</i>	HIV infection	Phase I (302) 498-6700
KP-1461	Koronis Pharmaceuticals <i>Redmond, WA</i>	HIV infection treatment	Phase II (425) 825-0240
nonakine (CCR5 antagonist)	Gryphon Therapeutics <i>South San Francisco, CA</i>	HIV infection treatment	Phase I (650) 952-7714
PA-1050040	Panacos Pharmaceuticals <i>Watertown, MA</i>	HIV infection	Phase I (617) 926-1551
PEHRG214	Virionyx <i>Auckland, New Zealand</i>	HIV-1 infection	Phase II www.virionyx.com
PF-232798	Pfizer <i>New York, NY</i>	HIV infection	Phase II (860) 732-5156

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
PPL-100 (PI)	Ambrilia Biopharma <i>Verdun, QC</i> Merck <i>Whitehouse Station, NJ</i>	HIV infection treatment	Phase I (800) 672-6372
PRO 140	Progenics Pharmaceuticals <i>Tarrytown, NY</i>	HIV infection treatment	Phase I (914) 789-2800
PRO 2000	Indevus Pharmaceuticals <i>Lexington, MA</i>	HIV infection prevention (intravaginal gel)	Phase III (781) 861-8444
Racivir [®] PSI-5004 (NRTI)	Pharmasset <i>Princeton, NJ</i>	HIV infection treatment	Phase II (609) 613-4100
RDEA-806 (NNRTI)	Ardea Biosciences <i>Carlsbad, CA</i>	HIV infections	Phase I (760) 602-8422
Reyataz [®] atazanavir (PI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	boosted naive HIV infection ----- HIV infection (pediatric)	in clinical trials (212) 546-4000 in clinical trials (212) 546-4000
rilpivirine (NNRTI)	Tibotec <i>Yardley, PA</i>	HIV-1 infection	Phase II (609) 730-7500
Selzentry [™] maraviroc	Pfizer <i>New York, NY</i>	HIV infection in treatment naive patients	Phase III (860) 732-5156
SP-01A (oral HIV entry inhibitor)	Pharmaplaz <i>Co. Roscommon, Ireland</i> Samaritan Pharmaceuticals <i>Las Vegas, NV</i>	HIV infection treatment	Phase II (702) 735-7001
Sustiva [®] efavirenz (NNRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection (pediatric)	in clinical trials (212) 546-4000
TAK-220 (CCR5 antagonist)	Tobira Therapeutics <i>Princeton, NJ</i>	HIV-1 infection	Phase I (781) 635-4346
TAK-652 (CCR5 antagonist)	Tobira Therapeutics <i>Princeton, NJ</i>	HIV-1 infection	Phase I (781) 635-4346
Tarvacin [™] bavituximab	Peregrine Pharmaceuticals <i>Tustin, CA</i>	HIV infection	Phase I (714) 508-6000
UC-781 (NNRTI)	Biosyn <i>Huntingdon Valley, PA</i> Cellegy Pharmaceuticals <i>Huntingdon Valley, PA</i>	HIV infection prevention	Phase I (215) 914-0900
UK-453061 (NNRTI)	Pfizer <i>New York, NY</i>	HIV infection	Phase II (860) 732-5156
VGX-1	Viral Genetics <i>Azusa, CA</i>	HIV infection treatment	in clinical trials (626) 334-5310
VGX-410	VGX Pharmaceuticals <i>Blue Bell, PA</i>	HIV infection	Phase II (267) 440-4200
vicriviroc (CCR5 receptor antagonist)	Schering-Plough <i>Kenilworth, NJ</i>	HIV infection	Phase III (908) 298-4000

GENE THERAPY

Product Name	Sponsor	Indication	Development Status
HGTV-43™ gene medicine	Enzo Therapeutics <i>Farmingdale, NY</i>	HIV-1 infection	Phase I (631) 755-5500
VRX496 (modified autologous T cells)	VIRxSYS <i>Gaithersburg, MD</i>	HIV infection treatment	Phase II (301) 987-0480

IMMUNOMODULATORS

Product Name	Sponsor	Indication	Development Status
AMZ-0026	Amazon Biotech <i>New York, NY</i>	HIV infection treatment	Phase II (212) 947-3363
AVR 118	Advanced Viral Research <i>Yonkers, NY</i>	AIDS-related cachexia	Phase II (914) 376-7383
		HIV infection treatment	Phase I (914) 376-7383
CYT 107 (recombinant interleukin-7)	Cytheris <i>Rockville, MD</i>	HIV infection	Phase I www.cytheris.com
Cytolin ® anti-CD8 mAb	CytoDyn <i>Santa Fe, NM</i>	HIV infection treatment	Phase II (505) 988-5520
PBS-119	Phoenix Biosciences <i>Hollywood, FL</i>	HIV infection	Phase I (954) 963-6647
Proleukin ® aldesleukin	Novartis Pharmaceuticals <i>East Hanover, NJ</i> National Institute of Allergy and Infectious Diseases (NIAID) <i>Bethesda, MD</i>	HIV-1 infection (see also anticancers)	Phase III (888) 669-6682

VACCINES

Product Name	Sponsor	Indication	Development Status
ADVAX (HIV DNA 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
AGS-004 (autologous dendritic cell vaccine)	Argos Therapeutics <i>Durham, NC</i>	HIV infection	Phase I (919) 287-6300
AVX-101 (single gene)	AlphaVax <i>Rsch. Triangle Park, NC</i>	HIV-1 infection	Phase I (919) 595-0400
DP-6001 (HIV DNA vaccine)	CytRx <i>Los Angeles, CA</i>	HIV-1 DNA vaccine with protein vaccine boost (prevention)	Phase I (310) 826-5648

VACCINES

Product Name	Sponsor	Indication	Development Status
EP1043	Pharmexa-Epimmune <i>San Diego, CA</i>	HIV infection	Phase I (858) 860-2500
EP1090 (HIV DNA vaccine)	Pharmexa-Epimmune <i>San Diego, CA</i>	HIV-1 infection	Phase I (858) 860-2500
EP1233 and MVA-BN polytope combination	Pharmexa-Epimmune <i>San Diego, CA</i> Bavarian Nordic <i>Washington, DC</i>	HIV infection prevention	Phase I (858) 860-2500 (202) 536-1581
gag DNA vaccine and IL-12 adjuvant	Wyeth <i>Collegeville, PA</i>	HIV infection, HIV infection prevention	Phase I (610) 902-1200
gag DNA vaccine and IL-15 adjuvant	Wyeth <i>Collegeville, PA</i>	HIV infection treatment	Phase I (610) 902-1200
		HIV infection prevention	Phase I (610) 902-1200
HIV DNA vaccine (LC002)	Genetic Immunity <i>McLean, VA</i> National Institute of Allergy and Infectious Diseases (NIAID) <i>Bethesda, MD</i>	HIV infection	Phase I (703) 883-0312
HIV recombinant vaccine	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection prevention	Phase I (888) 825-5249
HIV vaccine	GeoVax <i>Atlanta, GA</i>	HIV infection prevention	Phase I (404) 727-0971
HIV vaccine	Novartis Vaccines <i>Emeryville, CA</i>	HIV infection	Phase I (510) 655-8730
HIV vaccine	sanofi pasteur <i>Swiftwater, PA</i>	HIV infection prevention (Thailand)	Phase III (570) 839-4267
HIV vaccine (VRC-HIVADV-014)	GenVec <i>Gaithersburg, MD</i> NIAID Vaccine Research Center <i>Bethesda, MD</i>	HIV infection prevention	Phase II (240) 632-0740
		HIV infection treatment	Phase I (240) 632-0740
HIV vaccine (VRC-HIVDNA-016)	NIH Vaccine Research Center <i>Bethesda, MD</i>	HIV infection prevention	Phase II www.vrc.nih.gov
		HIV infection treatment	Phase I www.vrc.nih.gov
HIV vaccine (VRC-HIVADV-027)	GenVec <i>Gaithersburg, MD</i> NIH Vaccine Research Center <i>Bethesda, MD</i>	HIV infection prevention	Phase I (240) 632-0740
TBC-3B	Therion Biologics <i>Cambridge, MA</i> National Institutes of Health <i>Bethesda, MD</i>	HIV-1 infection	Phase I (617) 475-7500

VACCINES

Product Name	Sponsor	Indication	Development Status
tgAAC09	Targeted Genetics Seattle, WA International AIDS Vaccine Initiative New York, NY	HIV infection prevention	Phase II (206) 623-7612
V526	Merck Whitehouse Station, NJ	HIV infection	Phase II (800) 672-6372

OTHER

Product Name	Sponsor	Indication	Development Status
Enbrel® etanercept	Amgen Thousand Oaks, CA University of Wisconsin Madison, WI	advanced HIV-1 infection ----- cachexia	Phase I www.clinicaltrials.gov in clinical trials www.clinicaltrials.gov
ibalizumab (TNX-355)	Genentech South San Francisco, CA	HIV infection treatment	Phase II (650) 225-1000
Iplex™ mecasermin rinfabate	Insmed Richmond, VA	HIV-associated lipodystrophy	Phase II (804) 565-3000
Leukine® sargramostim	Bayer HealthCare Pharmaceuticals Wayne, NJ	HIV infection treatment	Phase III (888) 842-2937
Lyrica® pregabalin	Pfizer New York, NY	HIV-associated neuropathy	Phase III (860) 732-5156
Mexitil® mexiletine	Boehringer Ingelheim Pharmaceuticals Ridgefield, CT	HIV-associated peripheral nerve disorders	in clinical trials (800) 243-0127
NGX-4010 (high-concentration trans-capsaicin dermal patch)	NeurogesX San Carlos, CA	HIV-associated neuropathy	Phase III (650) 508-2116
PH284	Pherin Pharmaceuticals Redwood City, CA	AIDS-related cachexia	Phase II (650) 568-1587
Serostim® somatropin (rDNA origin) for injection (Orphan Drug)	EMD Serono Rockland, MA	HIV-associated adipose redistribution syndrome	application submitted (800) 283-8088
tesamorelin (TH9507)	Theratechnologies Saint-Laurent, Quebec	HIV-associated lipodystrophy	Phase III (514) 336-7800
Thalomid® thalidomide	Celgene Summit, NJ	AIDS-related cachexia (see also anticancers) ----- HIV infection treatment, <i>Mycobacterium avium</i> complex (MAC) infections	Phase III (908) 673-9000 Phase II (908) 673-9000

OTHER

Product Name	Sponsor	Indication	Development Status
TQ-1017	TheraQuest Biosciences <i>Blue Bell, PA</i>	HIV-associated neuropathy	Phase II (610) 272-2071
WinRho® SDF anti-D immunoglobulin	Baxter Healthcare <i>Deerfield, IL</i>	thrombocytopenia	Phase I (800) 422-9837

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
Agenerase® amprenavir (PI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i> Vertex Pharmaceuticals <i>Cambridge, MA</i>	HIV infection treatment
Aptivus® tipranavir (PI)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	advanced HIV-1 infection in combination with zidovudine
Atripla™ efavirenz 600mg/ emtricitabine 200mg/ tenofovir disoproxil fumarate 300mg (fixed-dose combination tablet)	Bristol-Myers Squibb <i>Princeton, NJ</i> Gilead Sciences <i>Foster City, CA</i>	HIV-1 infection in adults
Combivir® lamivudine/ zidovudine tablets (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection treatment
Crixivan® indinavir sulfate (PI)	Merck <i>Whitehouse Station, NJ</i>	HIV infection treatment
Emtriva® emtricitabine (FTC) (NRTI)	Gilead Sciences <i>Foster City, CA</i>	HIV infection in combination with other antiretroviral medications
Epivir® lamivudine (3TC) (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection treatment, HIV infection (once-daily dosing)
Epzicom™ lamivudine and abacavir sulfate (once-daily) (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <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

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
HIVID® zalcitabine (ddC) (NRTI)	Roche <i>Nutley, NJ</i>	in combination with other antiviral agents for treatment of HIV infection
Insentress™ raltegravir	Merck <i>Whitehouse Station, NJ</i>	in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents
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)
Lexiva™ fosamprenavir calcium (PI)	GlaxoSmithKline <i>Philadelphia, PA</i> <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
Rescriptor® delvaridine (NNRTI)	Pfizer <i>New York, NY</i>	HIV infection/AIDS
Retrovir® zidovudine (AZT) (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <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 sulfate (PI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	treatment of HIV-1 infection in combination with other antiretroviral medications
Selzentry™ maraviroc	Pfizer <i>New York, NY</i>	combination antiretroviral treatment of adults infected with only CCR5-tropic HIV-1 detectable who have evidence of viral replication and have HIV-1 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)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection treatment

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
Truvada™ emtricitabine/ tenofovir disoproxil fumarate	Gilead Sciences <i>Foster City, CA</i>	HIV infection in combination with other antiretroviral agents
VIDEX® didanosine (ddl) (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection, pediatric HIV infection, once-daily dosing
VIDEX® EC didanosine (ddl), enteric coated (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection
Viracept® nelfinavir mesylate (PI)	Pfizer <i>New York, NY</i>	HIV infection/AIDS (pediatric and adult)
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 (d4T) (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection, pediatric HIV infection, first-line in combination treatment
Ziagen® abacavir sulfate (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <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 public and industry sources and the Adis “R&D Insight” database based on the latest information. **Survey current as of November 6, 2007.** The information in this report 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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application submitted—Application for marketing has been submitted to the Food and Drug Administration (FDA).

candidiasis—A fungal (*Candida*) infection, usually of the moist cutaneous areas of the body, including the skin, mouth, esophagus and respiratory tract.

FI—Fusion inhibitor.

genital herpes—See **herpes simplex virus**.

herpes simplex virus—Three strains of the herpes virus often occur in AIDS patients: **Herpes simplex virus I (HSV I)**, which causes **cold sores** or fever blisters on the mouth or around the eyes and can be transmitted to the genital region. The latent virus can be reactivated by stress, trauma, other infections or suppression of the immune system to produce infection. **Herpes simplex II (HSV II)** causes painful sores of the anus or genitals. The virus may lie dormant in nerve tissue and can be reactivated to produce the sores. **Herpes varicella zoster virus (HVZ)**, also called **shingles**, consists of very painful blisters on the skin and affects areas innervated by specific nerves. It may appear in adulthood as a result of having had chicken pox (caused by the varicella virus) as a child.

histoplasmosis—A disease caused by a fungal infection that can affect all organs of the body.

HIV positive/infection/disease—Presence of antibodies in the blood to the human immunodeficiency virus (the virus that causes AIDS).

HIV-I refers to the most common strain of the virus found in U.S. AIDS patients.

immune thrombocytopenia purpura—A condition in which there is destruction of blood platelets by the immune system. The reduced number of platelets may result in abnormal bleeding into the skin (purpura) and other parts of the body.

immunocompromised—A condition in which the immune system fails to defend the body against infection and tumors.

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.

lymphoma—Cancers in which the cells of lymphoid tissue, found mainly in the lymph nodes and spleen, multiply unchecked. Lymphomas fall into two categories. One is Hodgkin's disease, characterized by a particular kind of abnormal cell. All others are **non-Hodgkin's lymphomas**, which vary in their malignancy according to the nature and activity of the abnormal cells and are most malignant when the cells are primitive or are poorly differentiated.

MAC/MAI—**MAC** refers to *Mycobacterium avium* complex. *Mycobacterium avium intracellulare* (**MAI**) is a bacterial infection that can affect most internal organs, resulting in widely disseminated disease in AIDS patients.

neuropathic pain—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.

PCP (*Pneumocystis carinii pneumonia*)—A type of lung infection rarely found in the general population but present in nearly 80 percent of all AIDS patients at some time during the course of the disease.

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.

prophylaxis—Treatment intended to preserve health and prevent the spread of disease.

wasting syndromes—Any number of conditions, such as **anorexia** and **cachexia**, resulting in a loss of body mass, notably protein.

SELECTED FACTS ABOUT HIV/AIDS*

	U.S. AIDS Cases through 2005 ¹	U.S. AIDS Deaths through 2005 ¹
Adults/Adolescents	975,043	545,529
Pediatric (under age 13)	9,112	4,865
TOTAL	984,155	545,529

HIV/AIDS Worldwide²

- An estimated 39.5 million people worldwide were living with HIV at the end of 2006. That year, an estimated 4.3 million people became newly infected with HIV and an estimated 2.9 million lost their lives to AIDS.
- Sub-Saharan Africa remains the worst-affected region in the world by the AIDS pandemic. A little more than one-tenth of the world's population live in sub-Saharan Africa, which is home to almost 64 percent of all people living with HIV—24.5 million. Two million of those people are children younger than age 15—almost 9 in 10 children living with HIV are in sub-Saharan Africa. In 2005, an estimated 2.7 million people in the region became newly infected with HIV, while 2 million adults and children died of AIDS. Some 12 million orphans were living in sub-Saharan Africa in 2005.
- New survey data underscore the disproportionate impact of the AIDS epidemic on women, especially in sub-Saharan Africa. Three-fourths of all women (age 15 and older) living with HIV are in that region of the world. Among young people (ages 15-24), that ratio widens considerably, to three young women for every one young man. The 13.2 million women living with HIV in sub-Saharan Africa represent 59 percent of all adults in that region who are living with the disease.
- An estimated 930,000 adults and children died of AIDS in southern Africa in 2005—one-third of all AIDS deaths globally.

HIV/AIDS in the United States (end of 2005)¹

- The estimated number of HIV/AIDS cases (in the 33 states with confidential name-based HIV infection reporting) decreased each year from 2001 through 2004, and then increased in 2005. At the end of that year, an estimated 475,220 people had been given a diagnosis and were living with HIV/AIDS. The largest number of cases occurred among people ages 35-39, accounting for 16 percent of all HIV/AIDS cases diagnosed in 2005.
- From 2001 through 2005, the estimated number of HIV/AIDS cases increased among whites, Asian/Pacific Islanders, and American Indian/Alaska Natives, while decreasing among African Americans and Hispanics. Despite the decrease among African Americans, they accounted for nearly half (49 percent) of all HIV/AIDS diagnoses in 2005.
- Through 2005, an estimated 249,950 people were reported as having HIV infection (not AIDS). By sex that year, 70 percent of the 35,107 reported cases of HIV infection (not AIDS) among adults and adolescents were in males and 30 percent were in females. In children, 430 cases of HIV infection (not AIDS) were reported.
- From 2000-2005, the estimated number of AIDS cases decreased 44 percent among children younger than age 13. That number also decreased among people in the age groups 30-34 and 35-39. The estimated number of AIDS cases increased among all racial and ethnic groups and among the following age groups: 15-19, 20-24, 25-29, 40-44, 45-49, 50-54, 55-59, 60-64, and 65 and older. The largest number of AIDS cases occurred among people ages 40-44, accounting for 20 percent of all AIDS cases diagnosed in 2005. That year, 93 AIDS cases were reported in children. The estimated number of AIDS cases increased 7 percent among females and 7 percent among males, who accounted for 73 percent of all AIDS cases diagnosed in 2005 among adults and adolescents.

* The term HIV/AIDS is used to refer to people with a diagnosis of HIV infection (not AIDS), a diagnosis of HIV infection and a later diagnosis of AIDS, or concurrent diagnoses of HIV infection and AIDS.

SELECTED FACTS ABOUT HIV/AIDS

HIV/AIDS in the United States (end of 2005)¹ (continued)

- At the end of 2005, an estimated 421,873 people in the United States were living with AIDS. By age group, most cases (23 percent) were in people ages 40-44, and by sex, the majority (77 percent) were male adults and adolescents. By race/ethnicity, 44 percent of people living with AIDS were African Americans, 35 percent were white, 19 percent Hispanic, 1 percent Asian/Pacific Islander, and less than 1 percent were American Indian/Alaska Natives.
 - The estimated number of U.S. AIDS deaths decreased 4 percent from 2001 through 2005. During that period of time, AIDS deaths among children younger than age 13 decreased as well as among those in the age groups 20-24, 25-29, 30-34, and 40-44. The estimated number of AIDS deaths remained stable among people ages 15-19, but it increased in the age groups 13-14, 45-49, 50-54, 55-59, 60-64, and 65 and older.
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Opportunistic Infections

- The use of combination antiretroviral therapy (ART) cut the rates of most opportunistic infections by about 80 percent. At first, this did not appear to be true for **AIDS-related non-Hodgkin lymphoma (NHL)**; however, newer studies show a decrease of about 50 percent in NHL rates, especially central nervous system (CNS) lymphoma. NHL still accounts for about 20 percent of the deaths of people with HIV. Approximately 10 percent of people with HIV may eventually develop NHL. The rate of NHL in people with HIV is more than 80 times higher than for the general population. The rate of NHL is also twice as high in men as in women and twice as high in Caucasians as in people of African or Caribbean ancestry.³
- ***Candida albicans*** is the most common **fungus** (yeast) in people with AIDS. It causes **candidiasis**, an infection that occurs mostly in the mouth and vagina (yeast infection). Candidiasis of the mouth (thrush) is the most common opportunistic infection in people with HIV. Infection of the esophagus with *C. albicans* is the most common AIDS-defining condition and is more common in women than in men.³
- Effective antiretroviral therapy has led to a marked reduction in **opportunistic fungal infections**. The incidence of such infections is now 20 percent to 25 percent of what it had been in the mid-1990s.³
- In the past, among men with AIDS, about 1 in 4 men who had sex with men developed **Kaposi's sarcoma (KS)** during their illness. That number is much smaller now because of the more effective treatment of HIV infection. Before the AIDS epidemic, KS was a rare disease. Its rate rose sharply by 1995, but now it has dropped to about one-seventh of what it was at its peak.⁴
- ***Mycobacterium avium complex (MAC)*** is a serious illness caused by a common bacterium found in water, soil, dust, and food. A healthy immune system will control MAC, but people with weakened immune systems can develop MAC disease. Up to 50 percent of people with AIDS may develop MAC, especially if their CD4 cell count is below 50.³
- Nearly one-third of people with HIV/AIDS experience some peripheral nerve damage (**peripheral neuropathy**), which can be caused by HIV itself, medications to treat the disease or complications, or as a result of opportunistic infections.⁵ Neuropathy is the most common cause of pain in those living with HIV.⁶
- ***Pneumocystis carinii pneumonia (PCP)*** became the leading AIDS-defining diagnosis in HIV-infected patients in the initial stages of the epidemic. PCP was responsible for two-thirds of AIDS-defining illnesses, and an estimated 75 percent of HIV-infected patients would develop PCP during their lifetime. The first substantial decline in the incidence of PCP occurred after the introduction of anti-PCP prophylaxis in 1989. The later use of combination antiretroviral therapy further reduced the rates of PCP among adults by 3.4 percent per year from 1992-1995. From 1996-1998, the rate of decline of PCP increased to 21.5 percent per year. Despite this improvement, PCP is still the most common AIDS-defining opportunistic infection in the United States. Today, almost 44 percent of PCP cases occur in patients not receiving medical care and in 41 percent of patients who either don't adhere to treatment or for whom the therapy doesn't work.¹

SELECTED FACTS ABOUT HIV/AIDS

Opportunistic Infections (continued)

- The United States has the highest **sexually transmitted disease (STD)** rates in the industrialized world.³ (STDs include human papillomavirus [HPV], trichomoniasis, chlamydia, genital herpes, gonorrhea, **HIV**, syphilis, and hepatitis B.) Nearly 19 million new STDs occurred in 2000. Although teens and young adults represent only 25 percent of the sexually active population, those ages 15 to 24 account for nearly half of all STD diagnoses each year. In 2000, more than 9 million new cases of STDs occurred among that age group: HPV, 4.6 million; trichomoniasis, 1.9 million; chlamydia, 1.5 million; genital herpes, 640,000; gonorrhea, 431,000; **HIV**, 15,000; syphilis, 8,200; and hepatitis B, 7,500.⁷
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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. 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).⁸
 - 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.⁹
 - Direct medical costs associated with **STDs** in the United States are estimated at \$13 billion annually. Excluding **HIV**, more than \$8 billion is spent each year to diagnose and treat STDs and their complications.⁷
 - The total estimated cost of the 9 million new **STD** cases among the 15- to 24-year-old age group was \$6.5 billion in year 2000 dollars. Viral STDs (genital herpes, **HIV**, hepatitis B, and human papillomavirus [HPV]) accounted for 94 percent (\$6.2 billion) of the total cost, while non-viral STDs (chlamydia, gonorrhea, syphilis, and trichomoniasis) accounted for the remaining 6 percent (\$0.4 billion). **HIV** and HPV were by far the most costly STDs, accounting for 90 percent (\$5.9 billion) of the total cost.⁷
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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. The Body, a service of Body Health Resources Corporation (www.thebody.com)
4. American Cancer Society (www.cancer.org)
5. The Jack Miller Center for Peripheral Neuropathy (www.millercenter.uchicago.edu)
6. NAM Publications (www.aidsmap.com)
7. Guttmacher Institute (www.guttmacher.com)
8. Medical News Today, MediLexicon International, Ltd. (www.medicalnewstoday.com)
9. PubMed Central, National Institutes of Health (www.pubmedcentral.nih.gov)

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
Years	6.5	Phase I	Phase II	Phase III	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 \$802 million to get one new medicine from the laboratory to U.S. patients, according to a November 2001 report 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 becomes effective if FDA does not disapprove it within 30 days. 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 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.

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 29 new therapeutics approved by the FDA in 2006 was 15.6 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. PhRMA member companies invested an estimated \$43 billion in research and development in 2006.

Medicines in Development for HIV/AIDS is presented by PhRMA in cooperation with the following organizations:

AIDS Project Los Angeles
AIDS Research Alliance
American Academy of Allergy, Asthma and Immunology
American College of Allergy, Asthma & Immunology
American Medical Directors Association
American Social Health Association
American Society for Microbiology
Association of Nurses in AIDS Care
Children's AIDS Fund
Citizens AIDS Project—CAVDA
Elizabeth Glaser Pediatric AIDS Foundation
Health Education Resource Organization (HERO)
Health Information Network/Seattle
HIV Medicine Association
Infectious Diseases Society of America
Interamerican College of Physicians & Surgeons
National Alliance for Hispanic Health
National Black Nurses Association
National Foundation for Infectious Diseases
National Medical Association
Planned Parenthood Federation of America
Title II Community AIDS National Network (T2CANN)
Women Alive Coalition

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