

HIV/AIDS

PRESENTED BY AMERICA'S PHARMACEUTICAL COMPANIES

Researchers Are Testing 79 Medicines and Vaccines For HIV and Opportunistic Infections

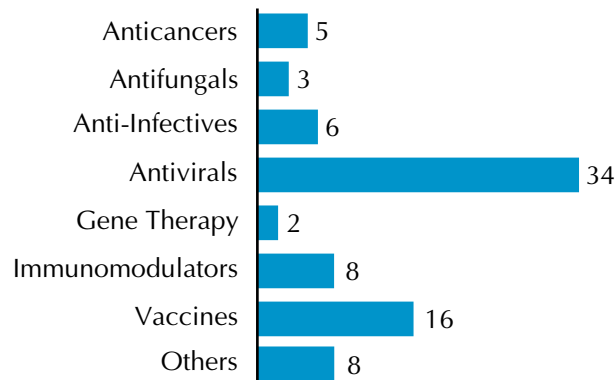
To better combat one of the world's most devastating diseases, pharmaceutical and biotechnology researchers are testing 79 medicines for HIV/AIDS and related conditions, intensifying their efforts and working toward the development of vaccines. The medicines now in the pipeline will add to the 82 that have already been approved since the virus that causes AIDS was first identified 20 years ago.

Vaccine research is considered crucial to control the AIDS pandemic. In what has been called "a silent revolution in AIDS vaccine research," 16 vaccines are in development.

AIDS has killed 28 million people and infected an estimated 42 million people worldwide, 70 percent of whom live in sub-Saharan Africa, where the pharmaceutical industry is making special efforts to counter the disease (see page 14). As many as 950,000 U.S. residents are estimated to be living with HIV infection, though the increased use of new medicines has helped to substantially reduce the AIDS death rate in this country in recent years. By 2010, it's estimated that 45 million new people could be infected with the HIV virus—unless there's a dramatic breakthrough. "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 Disease.

In addition to the 16 vaccines, the medicines in development for HIV/AIDS, which are either in human clinical trials or are at the Food and Drug Administration awaiting approval, include 34 antivirals, 6 anti-infectives, 5 cancer treatments, 8 immunomodulators, 3 antifungals, 2 gene therapies, and 8 other drugs.

Of the medicines and vaccines in development, one vaccine is designed to induce different types of immune response, enhancing the overall immune response. The first dose primes the body to induce cellular immunity. The booster dose, consisting of genetically engineered HIV subunits, induces neutralizing antibodies. Another vaccine candidate is made from a noninfectious copy of a protein from the surface of the AIDS virus. The vaccine is designed to induce an immune response through the production of antibodies that will prevent the invading virus from attaching to a patient's T-cells.

MEDICINES IN DEVELOPMENT FOR AIDS*

*Some medicines are listed in more than one category.

Examples of other AIDS medicines in the pipeline include:

- A protease inhibitor that, unlike other protease inhibitors, is not a peptide. The medicine, the first non-peptidic protease inhibitor with a unique chemical structure, has shown in clinical trials to reduce the levels of the virus in patients who have become resistant to other protease inhibitors.
- An antisense gene therapy that uses two novel technologies to boost immune responsiveness against HIV. One involves the insertion of a new type of genetic material into blood cells to inhibit the growth of the virus. The second involves inserting new genes into target cells and integrating the gene into the chromosome of the cell. The cells containing the new genes are then transferred to the patient.

While HIV/AIDS remains a formidable foe and worldwide scourge, pharmaceutical and biotechnology companies are meeting the challenge by continuing their all-out efforts to develop novel and more effective therapies and vaccines to contain the disease. We fully understand that patients all over the world are depending on them.

Alan F. Holmer
President and CEO
PhRMA

Medicines in Development for HIV/AIDS

ANTICANCERS

Product Name	Sponsor	Indication	Development Status*
Avastin™ bevacizumab	National Cancer Institute <i>Bethesda, MD</i> Genentech <i>South San Francisco, CA</i>	AIDS-related Kaposi's sarcoma	Phase II N C I T R I A L (800) 4-CANCER
BMS 275291 (MMPI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	AIDS-related Kaposi's sarcoma	Phase II (212) 546-4000
halofuginone	National Cancer Institute <i>Bethesda, MD</i> Collgard Biopharmaceuticals <i>Atlanta, GA</i>	AIDS-related Kaposi's sarcoma	Phase II N C I T R I A L (800) 4-CANCER
interleukin-12	National Cancer Institute <i>Bethesda, MD</i>	AIDS-related Kaposi's sarcoma	Phase I/II N C I T R I A L (800) 4-CANCER
Rituxan® rituximab	National Cancer Institute <i>Bethesda, MD</i> Biogen Idec <i>Cambridge, MA</i> Genentech <i>South San Francisco, CA</i>	HIV-associated lymphomas	Phase II N C I T R I A L (800) 4-CANCER

ANTIFUNGALS

Product Name	Sponsor	Indication	Development Status
DB 289	Immtech International <i>Vernon Hills, IL</i>	<i>Pneumocystis carinii</i> pneumonia (PCP) (see also anti-infectives)	Phase II (847) 573-0033
micafungin (FK463)	Fujisawa Healthcare <i>Deerfield, IL</i>	invasive fungal infections	application submitted (800) 727-7003
Noxafil posaconazole	Schering-Plough <i>Kenilworth, NJ</i>	opportunistic fungal infections	application submitted (908) 298-40000

ANTI-INFECTIVES

Product Name	Sponsor	Indication	Development Status
dapsone	Jacobus Pharmaceutical <i>Princeton, NJ</i>	<i>Pneumocystis carinii</i> pneumonia (PCP) prophylaxis	Phase III completed (609) 921-7447
dapsone and pyrimethamine and folinic acid	Jacobus Pharmaceutical <i>Princeton, NJ</i>	PCP and toxoplasmosis prophylaxis	Phase III completed (609) 921-7447
dapsone with trimethoprim	Jacobus Pharmaceutical <i>Princeton, NJ</i>	PCP treatment	Phase III completed (609) 921-7447

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

ANTI-INFECTIVES

Product Name	Sponsor	Indication	Development Status
DB 289	Immtech International <i>Vernon Hills, IL</i>	PCP (see also antifungals)	Phase II (847) 573-0033
GEM®92	Hybridon <i>Cambridge, MA</i>	HIV infection	Phase I completed (617) 679-5500
Ushercell cellulose sulfate	Polydex Pharmaceuticals <i>Toronto, Ontario</i>	prevention of HIV infection and other sexually transmitted diseases	Phase III (416) 755-2231

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
204937 (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection	Phase I (888) 825-5249
640385 (aspartyl protease inhibitor)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i> Vertex Pharmaceuticals <i>Cambridge, MA</i>	HIV infection	Phase I (888) 825-5249
695634 (NNRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection	Phase I (888) 825-5249
873140 (ONO-4128) (CCR5 antagonist)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection	Phase I (888) 825-5249
AG-1859	Pfizer <i>New York, NY</i>	HIV positive	Phase II (860) 732-0307
Alferon LDO®	Hemispherx Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	HIV infection (see also immunomodulators)	Phase I/II (888) 253-3766
AMD070	AnorMed <i>Langley, BC</i>	HIV infection	Phase I (604) 530-1057
Beta-L-Fd4C	Achillion Pharmaceuticals <i>West Haven, CT</i>	HIV infection	Phase II (203) 624-7000
calanolide A (NNRTI)	Sarawak MediChem Pharmaceuticals and Advanced Life Sciences <i>Woodbridge, IL</i>	HIV infection	Phase II (630) 739-6744
capravirine (NNRTI)	Pfizer <i>New York, NY</i>	HIV infection/AIDS	Phase II (860) 732-0307
CCR5 receptor antagonist	Schering-Plough <i>Kenilworth, NJ</i>	HIV infection	Phase II (908) 298-4000
Doxovir™	Redox Pharmaceutical <i>New York, NY</i>	HIV infection	Phase I (212) 543-4530
entecavir (BMS 200475)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV & hepatitis B co-infection	Phase III (212) 546-4000

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
IFN-alpha lozenge (natural human interferon-alpha) (Orphan Drug)	Amarillo Biosciences <i>Amarillo, TX</i>	treatment of oral warts in HIV-seropositive patients (see also immunomodulators)	Phase III (806) 376-1741, ext. 14
Kaletra [®] lopinavir/ritonavir (new dosing regimen)	Abbott Laboratories <i>Abbott Park, IL</i>	treatment of HIV infection	Phase III (847) 936-1189
KP-1461	Koronis Pharmaceuticals <i>Redmond, WA</i>	HIV infection/AIDS	Phase I (425) 825-0240
ME-609	Medivir <i>Huddinge, Sweden</i>	oral herpes	Phase II completed 46-8-608-3100
MIV-310	Medivir <i>Huddinge, Sweden</i>	multi-resistant HIV infection	Phase II 46-8-608-3100
PA-457	Panacos Pharmaceuticals <i>Gaithersburg, MD</i>	HIV infection	Phase II (240) 631-1395, ext. 300
PCL-016	Novactyl <i>St. Louis, MO</i> Upsher-Smith Laboratories <i>Maple Grove, MN</i>	herpes labialis (cold sores), herpes genitalis (genital herpes)	Phase II (800) 654-2299
PRO 140	Progenics Pharmaceuticals <i>Tarrytown, NY</i>	HIV infection	Phase I (914) 789-2800
PRO 542	Progenics Pharmaceuticals <i>Tarrytown, NY</i>	HIV infection	Phase II (914) 789-2800
PRO 2000	Indevus Pharmaceuticals <i>Lexington, MA</i>	prevention of HIV infection transmission (intravaginal gel)	Phase II/III (781) 861-8444
QR-437	Quigley Pharma <i>Doylestown, PA</i>	HIV infection	Phase I (267) 880-1100
Racivir [®]	Pharmasset <i>Tucker, GA</i>	HIV infection	Phase II (678) 395-0050
Reverset [™]	Incyte <i>Wilmington, DE</i> Pharmasset <i>Tucker, GA</i>	HIV infection	Phase II (302) 498-6700 (678) 395-0050
SPD754	Shire Pharmaceuticals <i>Rockville, MD</i>	HIV infection	Phase II (240) 453-6400
SPD756	Shire Pharmaceuticals <i>Rockville, MD</i>	HIV infection	Phase I (240) 453-6400
SPO1A	Samaritan Pharmaceuticals <i>Las Vegas, NV</i>	HIV infection	Phase II/III (702) 735-7001
tipranavir (PI)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	treatment of HIV-1 infection	application submitted (203) 798-4700
TMC114 (PI)	Tibotec <i>Yardley, PA</i>	HIV infection	Phase II

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
TMC125 (NNRTI)	Tibotec <i>Yardley, PA</i>	HIV infection	Phase II
UK-427,857	Pfizer <i>New York, NY</i>	HIV positive	Phase II (860) 732-0307
Valtrex™ XR valacyclovir (modified release)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	management of genital herpes (modified release)	Phase I (888) 825-5249

GENE THERAPY

Product Name	Sponsor	Indication	Development Status
HGTV43 (gene medicine)	Enzo Biochem <i>Farmingdale, NY</i>	HIV-1 infection	Phase I/II (631) 755-5500
TBC-M335+ TBC-M358+ TBC-F349+ TBC-F357	Therion Biologics <i>Cambridge, MA</i> NIAID <i>Bethesda, MD</i>	AIDS	Phase I

IMMUNOMODULATORS

Product Name	Sponsor	Indication	Development Status
Alferon LDO®	Hemispherx Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	HIV infection (see also antivirals)	Phase I/II (888) 253-3766
Ampligen®	Hemispherx Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	HIV infection (strategic treatment intervention)	Phase II (215) 988-0080
BAY 50-4798	Bayer Pharmaceuticals <i>West Haven, CT</i>	HIV infection	Phase I (800) 468-0894
IFN-alpha lozenge (natural human interferon-alpha) (Orphan Drug)	Amarillo Biosciences <i>Amarillo, TX</i>	treatment of oral warts in HIV-seropositive patients (see also antivirals)	Phase III (806) 376-1741, ext. 14
IMMUNITIN™ (HE2000)	Hollis-Eden Pharmaceuticals <i>San Diego, CA</i>	HIV infection/AIDS	Phase II (858) 587-9333
MDX-010	Medarex <i>Princeton, NJ</i>	HIV infection	Phase I/II (908) 479-2400
Remune® HIV-1 immunogen	Immune Response <i>Carlsbad, CA</i>	HIV seropositive	Phase II (760) 431-7080
SGN 00101	StressGen Biotechnologies <i>Victoria, British Columbia</i>	genital warts	Phase II (800) 661-4978

VACCINES

Product Name	Sponsor	Indication	Development Status
AG-702	Antigenics <i>New York, NY</i>	genital herpes	Phase I (212) 332-4774
AIDS vaccine	United Biomedical <i>Hauppauge, NY</i>	HIV infection	Phase I (631) 273-2828
ALVAC E120TMG	Aventis Pasteur <i>Swiftwater, PA</i>	HIV infection (Thailand)	Phase III (570) 839-4267
ALVAC MN120 TMGMP	Aventis Pasteur <i>Swiftwater, PA</i>	HIV disease	Phase I/II (570) 839-4267
AVX101 (HIV vaccine)	AlphaVax <i>Rsch. Triangle Park, NC</i>	HIV infection	Phase I (919) 595-0400
EP HIV-1090	Epimmune <i>San Diego, CA</i>	HIV-1 therapy	Phase I/II (858) 860-2515
genital herpes vaccine	AuRx <i>Glen Burnie, MD</i>	treatment of genital herpes	Phase I/II completed (410) 590-7610
HIV-1 DNA vaccine	Advanced Bioscience <i>Kensington, MD</i> CytRx <i>Los Angeles, CA</i>	HIV-1 DNA vaccine with protein vaccine boost	Phase I (508) 856-4182
HIV peptide vaccine	Wyeth <i>Philadelphia, PA</i>	prevention of HIV disease	Phase I
HIV recombinant vaccine	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection prophylaxis	Phase I (888) 825-5249
HIV vaccine	Chiron <i>Emeryville, CA</i> NIAID/VRC <i>Bethesda, MD</i>	HIV infection	Phase I www.hvtn.org
HIV vaccine	GeoVax <i>Atlanta, GA</i>	HIV infection	Phase I (404) 727-0971
HIV vaccine	Merck <i>Whitehouse Station, NJ</i>	prevention and treatment of HIV infection/AIDS	Phase I (800) 672-6372
recombinant vaccine	Therion Biologics <i>Cambridge, MA</i>	AIDS	Phase I (617) 475-7253
Simplirix recombinant vaccine	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	genital herpes prophylaxis	Phase III (888) 825-5249
VRC-HIVADV 014-00-VP (HIV vaccine)	GenVec <i>Gaithersburg, MD</i> NIAID/VRC <i>Bethesda, MD</i>	HIV infection	Phase I (240) 632-0740

OTHERS

Product Name	Sponsor	Indication	Development Status
AVR118	Advanced Viral Research <i>Yonkers, NY</i>	HIV infection	Phase I/II (914) 376-7383
buffer gel (microbicide)	ReProtect <i>Baltimore, MD</i>	prevention of sexual transmission of HIV infection	Phase II (410) 516-7260
HIV therapeutic	United Biomedical <i>Hauppauge, NY</i>	block progression from HIV infection to AIDS	Phase I (631) 273-2828
NGX-4010	NeurogesX <i>San Carlos, CA</i>	painful HIV-associated neuropathy	Phase II/III (650) 508-2116
Prosaptide™ prosaptide	Savient Pharmaceuticals <i>East Brunswick, NJ</i>	HIV-associated neuropathic pain	Phase II (800) 284-2480
rhIGF-1/rhIGFBP-3	Insmed <i>Richmond, VA</i>	AIDS lipodistrophy	Phase II (804) 565-3000
Serostim™ somatropin (rDNA origin) for injection (Orphan Drug)	Serono <i>Rockland, MA</i>	HIV-related adipose redistribution syndrome	Phase III (800) 283-8088
VRX496	VIRxSYS <i>Gaithersburg, MD</i>	HIV infection	Phase I

The content of this survey has been obtained through government and industry sources based on the latest information. **Survey current as of November 12, 2004.** The information may not be comprehensive. For more specific information about a particular product, contact the individual company directly. The entire series of "Medicines in Development" is available on PhRMA's web site.

PhRMA Internet address: <http://www.phrma.org>

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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/AIDS
Combivir® lamivudine/ zidovudine tablets (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection
Crixivan® indinavir sulfate (PI)	Merck <i>Whitehouse Station, NJ</i>	HIV infection
Emtriva® emtricitabine (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> BioChem Pharma <i>Laval, Quebec</i>	HIV infection, 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
Fortovase® saquinavir mesylate (PI) (soft gel formulation)	Roche <i>Nutley, NJ</i>	treatment of HIV infection in adults in combination with other antiretroviral agents
Fuzeon® enfuvirtide	Roche <i>Nutley, NJ</i> Trimeris <i>Durham, NC</i>	in combination with other antiretroviral agents for HIV infection
Gamimune®-N immune globulin intravenous (human)	Bayer <i>Berkeley, CA</i>	pediatric HIV infection
HIVID® zalcitabine (NRTI)	Roche <i>Nutley, NJ</i>	in combination with other antiviral agents for treatment of HIV infection
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

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
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)
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
Sustiva® efavirenz (NNRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection
Sustiva® efavirenz (once-daily) (NNRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection
Trizivir® abacavir, lamivudine and zidovudine combination tablet (NRTI)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection treatment
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) (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection
Viracept® nelfinavir mesylate (PI)	Agouron Pharmaceuticals, a Pfizer Company <i>La Jolla, CA</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

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
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
Zerit® XR stavudine (d4T) (NRTI)	Bristol-Myers Squibb <i>Princeton, NJ</i>	treatment of HIV infection in combination with other antiretrovirals
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

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
ABELCET® amphotericin B lipid complex	The Liposome Company <i>Princeton, NJ</i>	treatment of severe systemic fungal infections in patients refractory to or intolerant of amphotericin B therapy
Abreva™ docosanol 10% cream	Avanir Pharmaceuticals <i>San Diego, CA</i> GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	topical treatment for recurrent oral-facial herpes simplex infections
Alferon N Injection® interferon alfa-n3	Hemisphere Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	genital warts (<i>condyloma acuminata</i>)
AmBisome® liposomal amphotericin B	Fujisawa Pharmaceutical <i>Deerfield, IL</i> Gilead Sciences <i>Foster City, CA</i>	primary treatment for fever of unknown origin in neutropenic patients, visceral leishmaniasis, secondary treatment for certain systemic fungal infections, cryptococcal meningitis, histoplasmosis
Amphotec® amphotericin B cholesteryl sulfate lipid for injection	InterMune <i>Brisbane, CA</i>	aspergillosis, opportunistic systemic fungal infections
Bactrim™ sulfamethoxazole and trimethoprim	Women First HealthCare <i>San Diego, CA</i>	PCP prophylaxis and treatment
Bexxar® tositumomab	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	non-Hodgkin's lymphoma
Biaxin™ clarithromycin	Abbott Laboratories <i>Abbott Park, IL</i>	<i>Mycobacterium avium</i> complex (MAC) prophylaxis and treatment
Cancidas® casposfungin acetate	Merck <i>Whitehouse Station, NJ</i>	treatment of invasive aspergillosis in patients who are refractory to or intolerant of other therapies

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
Cytovene® ganciclovir (IV)	Roche <i>Nutley, NJ</i>	CMV retinitis treatment of immunocompromised patients and patients with AIDS
Cytovene® ganciclovir (oral)	Roche <i>Nutley, NJ</i>	CMV retinitis maintenance treatment, CMV retinitis prophylaxis in AIDS patients
Daraprim® pyrimethamine	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	toxoplasmosis treatment
DaunoXome® daunorubicin citrate liposome injection	Gilead Sciences <i>Foster City, CA</i>	advanced AIDS-related Kaposi's sarcoma
DepoCyt™ cytarabine liposome injection	SkyePharma <i>San Diego, CA</i>	neoplastic meningitis
Diflucan® fluconazole	Pfizer <i>New York, NY</i>	cryptococcal meningitis, candidiasis, pediatric use for candidiasis fungal infection prophylaxis and treatment
DOXIL® doxorubicin HCl liposome injection	ALZA Corporation <i>Palo Alto, CA</i>	AIDS-related Kaposi's sarcoma
Famvir® famciclovir	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	recurrent herpes simplex, including infections in HIV-infected patients
Foscavir® foscarnet sodium injection	AstraZeneca <i>Wilmington, DE</i>	CMV retinitis in AIDS patients, acyclovir-resistant herpes simplex virus (HSV) in immunocompromised patients
Intron® A interferon alfa-2b (recombinant)	Schering-Plough <i>Kenilworth, NJ</i>	AIDS-related Kaposi's sarcoma
Marinol® Capsules dronabinol	Solvay Pharmaceuticals <i>Marietta, GA</i>	treatment of anorexia associated with weight loss in AIDS patients and for the treatment of refractory nausea and vomiting associated with cancer chemotherapy
Megace® megestrol acetate (oral suspension)	Bristol-Myers Squibb <i>Princeton, NJ</i>	treatment of anorexia and cachexia associated with AIDS
Mepron® atovaquone	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	treatment of mild to moderate PCP in individuals intolerant to TMP/SMX; PCP prophylaxis
Mycobutin® rifabutin	Pfizer <i>New York, NY</i>	MAC prophylaxis in patients with advanced HIV infection
NebuPent® aerosol pentamidine isethionate	Fujisawa Healthcare <i>Deerfield, IL</i>	PCP prophylaxis
Neutrexin™ trimetrexate glucuronate for injection	MedImmune Oncology <i>Gaithersburg, MD</i>	treatment of moderate-to-severe PCP in immunocompromised patients, including patients with AIDS, who are intolerant of or are refractory to TMP/SMX or for whom TMP/SMX is contraindicated

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
Nizoral® 2% Shampoo ketoconazole	Janssen Pharmaceutica <i>Titusville, NJ</i>	tinea versicolor (fungal infection)
Nizoral® Tablets ketoconazole	Janssen Pharmaceutica <i>Titusville, NJ</i>	systemic fungal infections (blastomycosis, candidiasis, chronic mucocutaneous candidiasis, chromomycosis, coccidioidomycosis, histoplasmosis, oral thrush, paracoccidioidomycosis)
Ontak® denileukin diftitox	Ligand Pharmaceuticals <i>San Diego, CA</i>	non-Hodgkin's lymphoma
Onxol™ paclitaxel	IVAX Pharmaceuticals <i>Miami, FL</i>	AIDS-related Kaposi's sarcoma
Oxandrin® oxandrolone	Bio-Technology General <i>East Brunswick, NJ</i>	treatment of involuntary weight loss due to severe trauma, chronic infection, extensive surgery or unknown pathophysiology
Panretin® Capsules alitretinoin	Ligand Pharmaceuticals <i>San Diego, CA</i>	AIDS-related Kaposi's sarcoma
Panretin® Gel alitretinoin	Ligand Pharmaceuticals <i>San Diego, CA</i>	AIDS-related Kaposi's sarcoma
PASER™ Extended Release Granules para-aminosalicylic acid 4-aminosalicylic acid (PAS)	Jacobus Pharmaceutical <i>Princeton, NJ</i>	tuberculosis treatment
Pentam® 300 pentamidine isethionate (IM & IV)	Fujisawa Healthcare <i>Deerfield, IL</i>	PCP treatment
Priftin® rifapentine	Aventis Pharmaceuticals <i>Bridgewater, NJ</i>	tuberculosis
PROCRIT® epoetin alfa tablet	Ortho Biotech <i>Raritan, NJ</i>	anemia in Retrovir® -treated HIV-infected patients
Prosorba® Column protein A immunoadsorption	Cypress Bioscience <i>San Diego, CA</i>	immune thrombocytopenia purpura
Roferon®-A interferon alfa-2a, recombinant	Roche <i>Nutley, NJ</i>	Kaposi's sarcoma in patients 18 years of age or older
Septra® trimethoprim and sulfamethoxazole	Monarch Pharmaceuticals <i>Bristol, TN</i>	PCP prophylaxis and treatment
Serostim® somatropin (rDNA origin) for injection	Serono <i>Norwell, MA</i>	treatment of AIDS-associated cachexia (AIDS wasting)
Sporanox® Capsules itraconazole	Janssen Pharmaceutica <i>Titusville, NJ</i>	histoplasmosis, blastomycosis, second-line aspergillosis

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
Sporanox® Injection itraconazole	Janssen Pharmaceutica <i>Titusville, NJ</i>	systemic mycoses
Sporanox® Oral Solution itraconazole	Janssen Pharmaceutica <i>Titusville, NJ</i>	esophageal and oropharyngeal candidiasis
Taxol® paclitaxel	Bristol-Myers Squibb <i>Princeton, NJ</i>	AIDS-related Kaposi's sarcoma
Trovan™ trovafloxacin	Pfizer <i>New York, NY</i>	nosocomial pneumonia
Valcyte valganciclovir	Roche <i>Nutley, NJ</i>	AIDS-related CMV retinitis
Valtrex™ valacyclovir	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	episodic treatment of recurrent genital herpes and herpes zoster in immunocompetent adults, suppression of genital herpes simplex virus (HSV), suppression of HSV in immunocompromised patients, prevention of HSV transmission, suppression of recurrent genital herpes in HIV-infected individuals, reduction of risk of transmission of genital herpes in otherwise healthy, heterosexual adults
Vfend® voriconazole	Pfizer <i>New York, NY</i>	serious fungal infections
Vistide® cidofovir injection	Gilead Sciences <i>Foster City, CA</i>	CMV retinitis in AIDS patients
Vitravene™ fomivirsen	Isis Pharmaceuticals <i>Carlsbad, CA</i>	CMV retinitis in AIDS patients
WinRho SD™ Rh ₀ (D) immune globulin intravenous (human)	Nabi <i>Boca Raton, FL</i>	immune thrombocytopenic purpura (ITP) secondary to HIV infection
Zithromax® azithromycin	Pfizer <i>New York, NY</i>	<i>Mycobacterium avium intracellulare</i> (MAI) infections (prophylaxis)
Zovirax® acyclovir	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	herpes zoster/simplex, treatment of initial episodes and management of recurrent episodes of genital herpes, treatment of chicken pox and shingles

In collaboration with local non-governmental organizations and international health and relief groups, pharmaceutical companies are working to improve public health in the developing world. From 1998 through 2003, the pharmaceutical industry provided more than \$4.1 billion in financial assistance and medical products to developing nations. These programs represent long-term commitments to form global partnerships to help patients in these countries.

In addition to the medicines in development to treat HIV infection and related conditions, pharmaceutical companies are helping the developing world combat HIV infection and AIDS in several ways.

HIV/AIDS afflicts an estimated 39 million adults and three million children worldwide, and more than 70 percent of the afflicted people live in sub-Saharan Africa. According to the World Health Organization, today AIDS is the leading cause of death in Africa and the fourth worldwide. Pharmaceutical companies are working in a variety of ways to fight HIV/AIDS in Africa and other parts of the developing world.

What companies are doing:

- Through the *Accelerating Access Initiative*, several companies are selling AIDS medicines in developing countries at deeply discounted prices. Other companies are selling medicines at or below cost.
- One company is giving a medicine to treat deadly opportunistic fungal infections free to patients in South Africa and other developing nations.
- One company is supplying a protease inhibitor free of charge to prevent mother-to-child transmission of AIDS in developing nations.
- One company has established the *Academic Alliance for AIDS Care and Prevention in Africa* and will fund a clinic that will be operated by the alliance in partnership with Makerere University in Uganda.
- Through the Elizabeth Glaser Pediatric AIDS Foundation, one company donated \$1 million in grants to hospitals and universities in Africa to reduce mother-to-child transmission of the virus.
- *Secure the Future*, a program to address the needs of women and children affected by AIDS in South

and West Africa was set up by one company. The program includes community outreach, education and research.

- A pharmaceutical company-funded program known as *Step Forward ...for the world's children* works to improve the lives of AIDS orphans and vulnerable children in Tanzania, Burkina Faso, India, and Romania.
- One company has joined with the Bill & Melinda Gates Foundation to improve HIV/AIDS education, care and treatment in Botswana. The company has donated more than \$50 million worth of antiretroviral medicines.
- With a \$5 million grant, one company has funded the *Enhancing Care* initiative program for people living with HIV/AIDS in developing countries.
- One company actively supports SHARE, a multinational program that teaches doctors, health care workers, resource planners and public health experts about prevention and management of HIV.
- One company provides rapid HIV tests and anti-retroviral drugs in Africa and the 49 least developed countries (LDC); 20 million tests were pledged to programs for the prevention of mother to child transmission of HIV.
- A company pledged \$20 million in a partnership with Tanzania to build the country's AIDS response system.
- Through *Positive Action*, one company enhances the capacity of community organizations in 27 nations to deliver HIV education, prevention, care and support, and eliminate stigma/discrimination.
- One company supports training in China, Thailand and other countries on touch/massage therapy for orphaned/abandoned HIV-infected babies and children.
- One company has extended indefinitely a program that offers training and free medicine in Africa and Haiti to combat opportunistic infections associated with AIDS.

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

aspergillosis—Infection caused by aspergillus, a fungus sometimes found in old buildings or decaying plant matter.

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

CMV (cytomegalovirus)—This is sexually transmitted and can occur without symptoms or may result in mild flu-like symptoms. As an opportunistic infection in AIDS patients, it can cause **CMV retinitis**, an inflammation of the retina that can lead to blindness if left untreated.

cryptococcal meningitis—A fungal infection affecting the three membranes (meninges) surrounding the brain and spinal cord.

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

genital warts (*condyloma acuminata*)—Soft warts that grow in and around the entrance of the vagina and the anus and on the penis. They are transmitted by sexual contact and are caused by a **human papillomavirus**.

hepatitis—Inflammation of the liver with accompanying liver cell damage or death, caused most often by viral infection, e.g., **hepatitis B**, but also by certain drugs, chemicals or poisons. Hepatitis may be either acute (of limited duration) or chronic (continuing). **Hepatitis B virus (HBV)** can be transmitted through contaminated blood or blood products.

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.

human papillomavirus (HPV)—More than 60 types of HPV have been identified. Some types of the virus cause common skin warts. Other low-risk types of HPV cause **genital warts**. High-risk types of HPV cause cervical cancer and other genital cancers. HPV is one of the most common causes of **STDs** in the world.

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.

IM—Intramuscular.

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

IV—Intravenous.

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.

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 testing and identification of side effects in humans.

Phase III—Extensive clinical trials in humans to verify effectiveness and monitor adverse reactions.

PI—Protease inhibitor.

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

TMP/SMX—Refers to **trimethoprim-sulfamethoxazole**, an approved drug therapy for preventing and treating PCP.

toxoplasmosis—A disease due to infection with the protozoa *Toxoplasma gondii*, frequently causing focal encephalitis (inflammation of the brain).

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 December 2002 ¹	U.S. AIDS Deaths through December 2002 ¹
Adults/Adolescents	849,780	496,598
Pediatric (under age 13)	9,074	5,071
TOTAL	816,149	501,669

HIV/AIDS Worldwide²

- At the end of 2003, an estimated 37.8 million people worldwide—35.7 million adults and 2.1 million children younger than age 15—were living with **HIV/AIDS**. About two-thirds (25 million) of these people live in sub-Saharan Africa; another 20 percent (7.4 million) live in Asia and the Pacific. Women account for nearly half of all people worldwide living with HIV/AIDS.
- An estimated 4.8 million new **HIV infections** occurred worldwide during 2003—about 14,000 infections each day. More than 95 percent of these new infections were in developing countries. Also that year, some 6,000 young people ages 15 to 24 became infected with HIV every day.
- In 2003 alone, **HIV/AIDS-associated illnesses** caused the deaths of about 2.9 million people worldwide, including an estimated 490,000 children younger than age 15.

HIV/AIDS in the United States

- The Centers for Disease Control and Prevention (CDC) estimate that 850,000 to 950,000 U.S. residents are living with HIV infection, one-fourth of whom are unaware of their infection.²
- Approximately 40,000 new HIV infections occur each year in the United States: about 70 percent among males and 30 percent among females. Half of these newly infected people are younger than age 25.²
- Fewer than half of all HIV-infected American adults receive regular medical care. Only one-third of all HIV-infected Americans have private insurance, while fully one-fifth is uninsured. Public insurance—Medicaid and Medicare—covers the remaining half.³
- HIV transmission from mother to child during pregnancy, labor, and delivery or by breast-feeding has accounted for 91 percent of all AIDS cases reported among U.S. children. During the early 1990s, before perinatal preventive treatments were available, an estimated 1,000 to 2,000 U.S. infants were born with HIV infection annually. Between 1992 and 2002, perinatally acquired AIDS cases declined 90 percent in the United States, from 912 cases to 90 cases.¹
- Diagnoses of HIV/AIDS increased 3.2 percent from 2001 (25,643) to 2002 (26,464). The age group 25-34 represented 28 percent of all new diagnoses of HIV/AIDS. Although the rate of diagnoses remained stable among African Americans, in 2002 they accounted for 54 percent of all new diagnoses. That year, 71 percent of all new HIV/AIDS diagnoses occurred in men.¹
- In 2001, 39 percent of all HIV infections progressed to AIDS within 12 months after the HIV diagnosis.¹
- AIDS incidence increased throughout the 1980s, declined from the mid-1990s through 2001, and increased 2 percent in 2002 (compared with 2001). The age group 35-44 represented 41 percent of all new diagnoses of AIDS in 2002. The number of AIDS diagnoses increased 7 percent among women and decreased 5 percent among men from 1998 through 2002. That year, men accounted for 74 percent of all new AIDS diagnoses among U.S. adults.¹
- AIDS prevalence continued to increase over the period 1998-2002. At the end of 2002, an estimated 384,906 people in the United States were known to be living with AIDS. Of those, 42 percent were in the age group 35-44; 50 percent were black, 38 percent white, 10 percent Hispanic; and 73 percent were men.¹

SELECTED FACTS ABOUT HIV/AIDS

HIV/AIDS in the United States (continued)

- The estimated number of deaths among people with AIDS declined 14 percent from 1998 (19,005) to 2002 (16,371).¹
-

Opportunistic Infections

- **Esophageal candidiasis** has been reported to be the most common opportunistic infection in developed countries, affecting up to 20 percent of AIDS patients.⁴
- Worldwide, **cryptococcosis** is the second or third most common opportunistic infection in HIV/AIDS.²
- Combination antiviral therapy has reduced the rate of **cytomegalovirus** (CMV) in people with HIV by 75 percent, yet about 5 percent of people with HIV still develop CMV.⁵
- The rates of opportunistic **fungal infections** in AIDS can range from 60 percent to 90 percent for mucosal **candidiasis** to 6 percent to 30 percent for invasive mycoses (such as **cryptococcosis**, **histoplasmosis** and **coccidioimycosis**).²
- **Hepatitis B** is the most common serious liver infection in the world and is 100 times more infectious than the AIDS virus. The CDC estimates that 1.25 million Americans are chronically infected with hepatitis B, and 100,000 people will become newly infected this year.⁶ Of those new cases, about half will be the result of sexual intercourse. In 1995, about one-third of people with acute hepatitis B virus infections had a history of another sexually transmitted disease.¹ Up to 6,000 people die of hepatitis B-related liver complications each year.⁶
- **Hepatitis C virus (HCV)** is the most common chronic bloodborne infection in the United States. Some 4 million people have been infected with HCV. Up to 85 percent of the people infected with HCV each year will develop chronic infection.⁷
- In 1999, the CDC added **HCV infection** to the list of opportunistic infections associated with **HIV**. Up to one-fourth of HIV-positive individuals in this country are co-infected with HCV. Since 2000, HCV-related end-stage liver disease has been recognized as a leading cause of death among people with HIV.⁸ One study found that more than 40 percent of deaths in HIV-positive individuals were associated with liver disease either as a primary or associated cause of death.⁹
- Transmission of **HCV** to offspring among mothers with HCV infection alone is estimated to be about 2 percent, but rates two to three times as high have been reported among those with both HCV and HIV infection.¹⁰
- **Genital herpes** affects an estimated 1 out of 4 (or 45 million) Americans, with about 500,000 new cases developing annually.¹
- Health experts estimate that there are more cases of genital **human papillomavirus** (HPV) infection than of any other sexually transmitted disease (STD) in the United States. Approximately 5.5 million new cases of sexually transmitted HPV infections are reported every year, and as many as 24 million Americans are already infected.²
- About two-thirds of people who have sexual contact with a partner who has **genital warts** (caused by low-risk types of **HPV**) usually develop warts themselves within three months of contact.²
- In the past, about 1 in 4 homosexual or bisexual males with AIDS developed **Kaposi's sarcoma** (KS). Today, because of more effective HIV treatments, the rate of KS among that population has dropped to about one-seventh of what it was at its peak.¹¹
- **AIDS-related lymphoma** is sometimes called **non-Hodgkin's lymphoma** (NHL). About 10 percent of people with **HIV** may eventually develop NHL. The rate of lymphoma in people with HIV is over 80 times higher than for the general population. Some new studies have shown a decrease of about 40 percent in NHL rates in HIV patients due to combination antiviral therapy, but lymphoma still accounts for the deaths of about 20 percent of people with HIV.⁵

SELECTED FACTS ABOUT HIV/AIDS

Opportunistic Infections (continued)

- **Pneumocystis carinii pneumonia (PCP)** is the most common opportunistic infection in people with HIV. Without treatment, more than 85 percent of people with HIV would eventually develop PCP. Between 1991 and 1997, there was a 36 percent drop in the number of PCP cases in the United States, and since people started taking combination antiviral therapy, the number of cases has dropped even further. PCP was the first AIDS-defining diagnosis for only 32 percent of cases in 1993 compared to 63 percent in 1987. PCP was the cause of death for 14 percent of people with AIDS in 1993 compared to 32 percent in 1987.⁵
 - The United States has the highest rates of **sexually transmitted diseases (STDs)**, including **HIV/AIDS, gonorrhea, genital herpes, human papillomavirus** and **hepatitis B** in the industrialized world—50 to 100 times higher. An estimated 15.3 million new cases of STDs are reported each year in this country. Health problems caused by STDs tend to be more severe for women than for men.¹
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Costs

- The average lifetime cost per case of **genital herpes** is \$417 for women and \$511 for men. The total direct medical costs for the disease in 2000 were \$292.7 million.¹²
 - The average lifetime cost per case of **hepatitis B** is \$779. In 2000, the total direct medical costs for the disease were \$5.8 million.¹²
 - The 48-week course of treatment for **hepatitis C virus infection** costs an estimated \$40,000.⁸
 - Researchers estimate that the lifetime treatment cost for a person with **HIV** now averages about \$155,000. Estimates are that 40,000 people are infected yearly, resulting in an annualized cost of more than \$6 billion. The cumulative cost of lifetime treatment increases by more than \$6 billion yearly if the number of infections stays steady, as it has over the last decade. In the last five years alone, an estimated 200,000 people have been infected with HIV. Treating them over the rest of their lives will cost the nation \$31 billion.¹
 - In the United States, preventing mother-to-child **HIV** transmission costs about \$33,000 per infection averted. The total lifetime treatment cost for perinatally infected infants is estimated to be between \$51.8 million and \$68.5 million, assuming 280-370 perinatal infections per year and a lifetime cost of \$185,000 per infant.¹
 - The average lifetime cost per case of **human papillomavirus (HPV)** is \$1,228 for women and \$27 for men. In 2000, the total direct medical costs for HPV were \$2.9 billion.¹²
 - In 1994, the direct costs (such as expenditures for medical and non-medical services and materials) and indirect costs (mainly lost wages) of the major **STDs** (including **HIV/AIDS, herpes simplex, human papillomavirus** and **hepatitis B**) and their complications were estimated to total nearly \$17 billion annually.¹
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Sources:

1. U.S. Centers for Disease Control and Prevention (www.cdc.gov)
2. National Institute of Allergy and Infectious Diseases (www.niaid.nih.gov)
3. Rand Health (www.rand.org)
4. HIV InSite, a project of the University of California/San Francisco (www.hivinsite.ucsf.edu)
5. The Body: An AIDS and HIV Information Resource (www.thebody.com)
6. Hepatitis B Foundation (www.hepb.org)
7. American Liver Foundation (www.liverfoundation.org)
8. aidsinfonyc.org, Treatment Action Group (www.aidsinfonyc.org)
9. Reuters Health Information (www.hivandhepatitis.com)
10. MedReviews, LLC: "HCV and HIV: A Tale of Two Viruses," Kenneth E. Sherman, M.D., Ph.D., Division of Digestive Diseases, University of Cincinnati College of Medicine, Cincinnati, OH (www.medreviews.com)
11. American Cancer Society (www.cancer.org)
12. Focus on the Family (www.family.org)

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 1.5	Phase II 2	Phase III 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 to 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). Following the completion of all three phases of clinical trials, a company analyzes all of the data and files an NDA with FDA if the data successfully demonstrate both safety and effectiveness. The NDA contains all of the scientific information that the company has gathered. NDAs typically run 100,000 pages or more. The average NDA review time for 21 new molecular entities (NMEs) approved by the FDA in 2003 was 16.9 months.

Approval. Once FDA approves an NDA, 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 \$33.2 billion in research and development in 2003.

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

AIDS Action
AIDS Project Los Angeles
AIDS Research Alliance
American Academy of Allergy, Asthma and Immunology
American Academy of Physician Assistants
American Association of Immunologists
American College of Allergy, Asthma & Immunology
American Medical Directors Association
American Nurses Association
American Social Health Association
American Society for Microbiology
Association of Nurses in AIDS Care
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Elizabeth Glaser Pediatric AIDS Foundation
Foundation for Retrovirology and Human Health
Health Education Resource Organization (HERO)
Health Information Network/Seattle
Infectious Diseases Society of America
Interamerican College of Physicians & Surgeons
Mothers' Voices
National Alliance for Hispanic Health
National Black Nurses Association
National Foundation for Infectious Diseases
National Medical Association
National Native American AIDS Prevention Center
Office of AIDS Research, National Institutes of Health
Planned Parenthood Federation of America
Women Alive Coalition

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