

HIV/AIDS

PRESENTED BY AMERICA'S PHARMACEUTICAL COMPANIES

Researchers Are Testing 77 Medicines and Vaccines For HIV and Opportunistic Infections

HIV/AIDS is one of the world's most devastating diseases. To help fight it, biopharmaceutical researchers are testing 77 medicines for HIV/AIDS and related conditions and intensifying their work toward the development of vaccines. The medicines now in the pipeline will add to the 88 already approved since the AIDS virus was first identified more than 20 years ago.

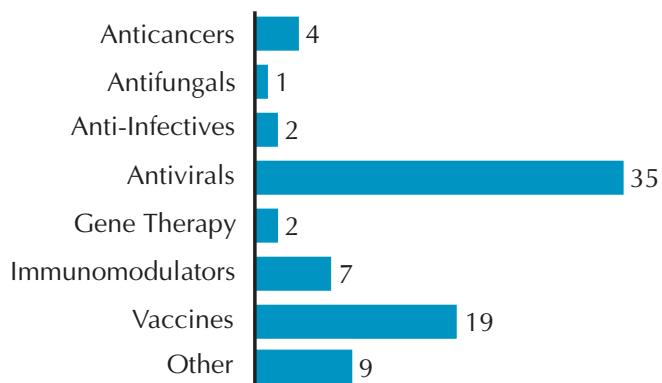
Vaccine research is crucial to the fight against AIDS. "A safe and effective HIV vaccine is critical to the control of HIV globally," says Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases. Currently, 19 vaccines are in development.

According to the Joint United Nations Programme on HIV/AIDS, over the last quarter century, nearly 65 million people were infected with HIV, and an estimated 25 million have died of AIDS-related illnesses. As many as 1.2 million U.S. residents are estimated to be living with HIV infection. Today it is estimated that close to 40 million people worldwide live with HIV—yet the vast majority are unaware of their status. The increased use of newer prescription medicines has helped in recent years to substantially reduce the U.S. AIDS death rate. However, without a dramatic breakthrough about 45 million new people could be infected with the HIV virus by 2010.

In addition to the 19 vaccines there are, 35 antivirals, two anti-infectives, four cancer treatments, seven immunomodulators, one antifungal, two gene therapies, and nine other medicines are now in human clinical trials or before the Food and Drug Administration awaiting approval.

Examples of AIDS medicines and vaccines in the pipeline include:

- One medicine, the first in a new class of drugs known as integrase inhibitors, has been shown to decrease viral load in patients with significant HIV drug resistance.
- A medicine in development binds itself to a receptor protein found on the surface of human cells and blocks the HIV virus from entering the cell.

MEDICINES IN DEVELOPMENT FOR AIDS*

*Some medicines are listed in more than one category.

- A vaccine combines DNA snippets from the AIDS virus with a protein that boosts immune response. The vaccine may prevent infection, limit the damage the virus causes, or both.
- An antisense gene therapy 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, research-based pharmaceutical and biotechnology 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*
Avastin® bevacizumab	National Cancer Institute <i>Bethesda, MD</i> Genentech <i>South San Francisco, CA</i>	AIDS-related Kaposi's sarcoma	Phase II NCI TRIAL (800) 4-CANCER
Nexavar® sorafenib	National Cancer Institute <i>Bethesda, MD</i> Bayer HealthCare, Pharmaceuticals <i>West Haven, CT</i>	AIDS-related Kaposi's sarcoma	Phase I NCI TRIAL (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>	AIDS-related lymphoma	Phase II NCI TRIAL (800) 4-CANCER
Thalomid® thalidomide	Celgene <i>Summit, NJ</i>	Kaposi's sarcoma (see also other)	Phase II (908) 673-9000

ANTIFUNGALS

Product Name	Sponsor	Indication	Development Status
Noxafil® posaconazole	Schering-Plough <i>Kenilworth, NJ</i>	treatment of oropharyngeal candidiasis	application submitted (908) 298-4000

ANTI-INFECTIVES

Product Name	Sponsor	Indication	Development Status
pafuramidine (DB289)	Immtech International <i>Vernon Hills, IL</i>	<i>Pneumocystis carinii</i> pneumonia (PCP)	Phase III (847) 573-0033
Ushercell® cellulose sulfate	Polydex Pharmaceuticals <i>Toronto, Ontario</i>	HIV infection prevention	Phase I (416) 755-2231

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
364735 (integrase inhibitor)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i> Shionogi USA <i>Florham Park, NJ</i>	HIV infection treatment	Phase I (888) 825-5249

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

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
Alferon LDO®	Hemispherx Biopharma New Brunswick, NJ Philadelphia, PA	HIV infection treatment (see also immunomodulators)	Phase II (888) 253-3766
AMD070	AnorMed Langley, British Columbia	HIV-1 infection	Phase I (604) 530-1057
amdoxovir (DAPD)	Emory University Atlanta, GA University of Georgia Atlanta, GA	HIV infection treatment	Phase II completed
apricitabine (AVX754)	Avexa Richmond, Australia	HIV-1 infection	Phase I www.avexa.com
bevirimat (PA-457)	Panacos Pharmaceuticals Watertown, MA	HIV infection treatment	Phase II (617) 926-1551
brecanavir (640385, aspartyl protease inhibitor)	GlaxoSmithKline Philadelphia, PA Rsch. Triangle Park, NC Vertex Pharmaceuticals Cambridge, MA	HIV infection	Phase II (888) 825-5249
calanolide A (NNRTI)	Sarawak MediChem Pharmaceuticals Woodridge, IL	HIV-1 infection	Phase I (630) 739-6744
CCR5 mAb	Human Genome Sciences Rockville, MD	HIV infection treatment	Phase I (301) 309-8504
CYT 99007 (recombinant interleukin-7)	Cytheris Rockville, MD	HIV infection	Phase I www.cytheris.com
elvucitabine (Beta-L-Fd4C)	Achillion Pharmaceuticals New Haven, CT Vion Pharmaceuticals New Haven, CT	HIV infection treatment	Phase II (203) 624-7000
etravirine (TMC125, NNRTI)	Tibotec Pharmaceuticals Co. Cork, Ireland Yardley, PA	HIV infection treatment	Phase III (609) 730-7500
fozivudine tidoxil	Heidelberg Pharma Ladenburg, Germany	HIV infection treatment	Phase II www.heidelberg-pharma.com
Fuzeon® enfuvirtide	Roche Nutley, NJ Trimeris Durham, NC	HIV-1 infection (once-daily dosing vs. twice-daily dosings)	Phase II (973) 235-5000
GS 9137	Gilead Sciences Foster City, CA	HIV infection treatment	Phase II (650) 574-3000
GS 9160	Gilead Sciences Foster City, CA	HIV infection	Phase I (650) 574-3000
HIV attachment inhibitor	Bristol-Myers Squibb Princeton, NJ	HIV-1 infection	Phase I (212) 546-4000

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
HRG214	Virionyx <i>Auckland, New Zealand</i>	HIV infection treatment	Phase II www.virionyx.com
INCB 9471	Incyte <i>Wilmington, DE</i>	HIV infection treatment	Phase I/II (302) 498-6700
KP-1461	Koronis Pharmaceuticals <i>Redmond, WA</i>	HIV infection treatment	Phase I (425) 825-0240
maraviroc (UK-427,857, CCR5 coreceptor antagonist)	Pfizer <i>New York, NY</i>	HIV-1 infection treatment	Phase III (860) 732-5156
MK-0518 (integrase inhibitor)	Merck <i>Whitehouse Station, NJ</i>	HIV-1 infection	Phase III (800) 672-6372
nonakine	Gryphon Therapeutics <i>South San Francisco, CA</i>	HIV infection treatment	Phase I (650) 952-7714
PBS119	Phoenix Biosciences <i>Hollywood, FL</i>	HIV infection	Phase I (954) 963-6647
PRO 140	Progenics Pharmaceuticals <i>Tarrytown, NY</i>	HIV infection treatment	Phase I (914) 789-2800
PRO 542 (CD4-IgG2)	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 [®] (NRTI)	Pharmasset <i>Princeton, NJ</i>	HIV infection treatment	Phase II (609) 613-4100
Reyataz [®] atazanavir (ATV) (300mg single- dose capsule)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection	application submitted (212) 546-4000
Reyataz [®] atazanavir (ATV) (oral powder)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection (pediatric)	Phase III (212) 546-4000
Reyataz [®] atazanavir (400mg QD or 300mg QD with 100mg Norvir [®] ritonavir) (oral capsule)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV infection in antiretroviral-boosted naive patients	Phase III (212) 546-4000
SP-01A	Samaritan Pharmaceuticals <i>Las Vegas, NV</i>	HIV infection treatment	Phase II (702) 735-7001
Sustiva [®] efavirenz (oral solution)	Bristol-Myers Squibb <i>Princeton, NJ</i>	HIV-1 infection (pediatric)	Phase II (212) 546-4000
VGX-410	VGX Pharmaceuticals <i>Blue Bell, PA</i>	HIV infection	Phase II (267) 440-4200

ANTIVIRALS

Product Name	Sponsor	Indication	Development Status
vicriviroc (CCR5 receptor antagonist)	Schering-Plough <i>Kenilworth, NJ</i>	HIV-1 infection	Phase II (908) 298-4000

GENE THERAPY

Product Name	Sponsor	Indication	Development Status
HGTV-43™ gene medicine	Enzo Biochem <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
Alferon LDO®	Hemispherx Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	HIV infection treatment (see also antivirals)	Phase II (888) 253-3766
Ampligen®	Hemispherx Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	HIV infection treatment (strategic treatment intervention)	Phase II/III (215) 988-0080
AMZ0026	Amazon Biotech <i>New York, NY</i>	HIV infection treatment	Phase II (212) 947-3363
anti-HIV-1 mAb	Polymun Scientific <i>Vienna, Austria</i>	HIV infection treatment	Phase II www.polymun.com
BAY 50-4798	Bayer HealthCare Pharmaceuticals <i>West Haven, CT</i>	HIV infection treatment	Phase I/II (203) 812-2000
Cytolin® anti-CD8 mAb	CytoDyn <i>Santa Fe, NM</i>	HIV infection treatment	Phase II (505) 988-5520
IMMUNITIN™ HE 2000	Hollis-Eden Pharmaceuticals <i>San Diego, CA</i>	HIV infection treatment	Phase II (858) 587-9333

VACCINES

Product Name	Sponsor	Indication	Development Status
825780 (DNA antiviral vaccine)	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection treatment	Phase I (888) 825-5249
ADVAX	Aaron Diamond AIDS Research Center <i>New York, NY</i> International AIDS Vaccine Initiative <i>New York, NY</i>	HIV infection prevention	Phase I completed (212) 448-5000 (212) 847-1111

VACCINES

Product Name	Sponsor	Indication	Development Status
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
EP 1043	Pharmexa-Epimmune <i>San Diego, CA</i>	HIV infection prevention	Phase I (858) 860-2500
EP 1090 (HIV DNA vaccine)	Pharmexa-Epimmune <i>San Diego, CA</i>	HIV-1 infection treatment	Phase I (858) 860-2500
GENEVAX (HIV DNA vaccine)	Wyeth <i>Collegeville, PA</i>	HIV infection treatment	Phase I (610) 902-1200
HIV DNA vaccine (pGA2/JS2)	Emory University <i>Atlanta, GA</i> National Institutes of Health <i>Bethesda, MD</i>	HIV infection prevention	Phase I www.clinicaltrials.gov
HIV recombinant vaccine	GlaxoSmithKline <i>Philadelphia, PA</i> <i>Rsch. Triangle Park, NC</i>	HIV infection prevention	Phase I (888) 825-5249
HIV therapeutic	sanofi pasteur <i>Swiftwater, PA</i>	HIV infection treatment (ART interruption)	Phase II (570) 839-4267
HIV vaccine	GeoVax <i>Atlanta, GA</i>	HIV infection prevention	Phase I (404) 727-0971
HIV vaccine	sanofi pasteur <i>Swiftwater, PA</i>	HIV infection prevention (Thailand)	Phase III (570) 839-4267
HIV vaccine	Novartis Vaccines <i>Emeryville, CA</i> National Institutes of Health <i>Bethesda, MD</i>	HIV infection	Phase I (510) 655-8730
HIV vaccine (VRC-HIVADV-009)	NIH Vaccine Research Center <i>Bethesda, MD</i>	HIV infection	Phase I www.clinicaltrials.gov
HIV vaccine (VRC-HIVADV-014)	GenVec <i>Gaithersburg, MD</i> NIH Vaccine Research Center <i>Bethesda, MD</i>	HIV infection prevention	Phase II (240) 632-0740
HIV vaccine (VRC-HIVDNA-016)	Dale and Betty Bumpers Vaccine Research Center at the National Institutes of Health <i>Bethesda, MD</i>	HIV infection prevention	Phase II www.vrc.nih.gov
TBC-3B	Therion Biologics <i>Cambridge, MA</i> National Institutes of Health <i>Bethesda, MD</i>	HIV-1 infection	Phase I (617) 475-7500
tgAAC09	Targeted Genetics <i>Seattle, WA</i> International AIDS Vaccine Initiative <i>New York, NY</i>	HIV infection	Phase II (206) 623-7612
V526	Merck <i>Whitehouse Station, NJ</i>	HIV-1 infection	Phase II/III (800) 672-6372

OTHER

Product Name	Sponsor	Indication	Development Status
dapivirine (TMC 120)	International Partnership for Microbicides <i>Silver Spring, MD</i>	HIV infection prevention	Phase I (301) 608-2221
Enbrel® etanercept	Amgen <i>Thousand Oaks, CA</i> University of Wisconsin <i>Madison, WI</i>	HIV-1 infection	Phase I www.clinicaltrials.gov
NGX-4010 (high-concentration trans-capsaicin dermal patch)	NeurogesX <i>San Carlos, CA</i>	painful HIV-associated neuropathy	Phase III (650) 508-2116
Savvy® 1% C31G vaginal gel (microbicide)	Biosyn <i>Huntingdon Valley, PA</i> Cellegy Pharmaceuticals <i>Huntingdon Valley, PA</i>	HIV infection prevention	Phase I (215) 914-0900
Serostim® somatropin (rDNA origin) for injection (Orphan Drug)	Serono <i>Rockland, MA</i>	lipodystrophy	application submitted (800) 283-8088
TH9507 (tesamorelin)	Theratechnologies <i>Saint-Laurent, Quebec</i>	lipodystrophy	Phase III (514) 336-7800
Thalomid® thalidomide	Celgene <i>Summit, NJ</i>	cachexia (see also anticancer)	Phase III (908) 673-9000
		HIV infection treatment, mycobacterium avium complex (MAC) infections	Phase II (908) 673-9000
TNX-355	Tanox <i>Houston, TX</i>	HIV infection treatment	Phase II (713) 578-4000
UC-781	Biosyn <i>Huntingdon Valley, PA</i> Cellegy Pharmaceuticals <i>Huntingdon Valley, PA</i>	HIV infection prevention	Phase I (215) 914-0900

The content of this survey has been obtained through the Adis "R&D Insight" database and industry sources based on the latest information. **Survey current as of October 2, 2006.** The information may not be comprehensive. For more specific information about a particular product, contact the individual company directly or go to www.clinicaltrials.gov. The entire series of "Medicines in Development" is available on PhRMA's web site.

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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
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
Crixivan® indinavir sulfate (PI)	Merck <i>Whitehouse Station, NJ</i>	HIV infection
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> 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 (FI)	Roche <i>Nutley, NJ</i> Trimeris <i>Durham, NC</i>	in combination with other antiretroviral agents for HIV infection
HIVID® zalcitabine (ddC) (NRTI)	Roche <i>Nutley, NJ</i>	in combination with other antiviral agents for treatment of HIV infection

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
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
Kaletra® lopinavir/ritonavir [new dosing (PI) regimen]	Abbott Laboratories <i>Abbott Park, IL</i>	treatment of HIV infection
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
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

APPROVED MEDICINES FOR HIV INFECTION/AIDS

Product Name	Company	Indication
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

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	Hemispherx Biopharma <i>New Brunswick, NJ</i> <i>Philadelphia, PA</i>	genital warts (<i>condyloma acuminata</i>)
AmBisome® liposomal amphotericin B	Astellas Pharma US <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

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
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
Candidas® casopfungin acetate	Merck <i>Whitehouse Station, NJ</i>	treatment of invasive aspergillosis in patients who are refractory to or intolerant of other therapies
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
Gamimune®-N immune globulin intravenous (human)	Bayer <i>Berkeley, CA</i>	immune booster to prevent bacterial infections in children with HIV infection
Intron® A interferon alfa-2b (recombinant)	Schering-Plough <i>Kenilworth, NJ</i>	AIDS-related Kaposi's sarcoma

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
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
Mycamine® micafungin sodium	Astellas Pharma US <i>Deerfield, IL</i>	prevention of <i>Candida</i> infections
Mycobutin® rifabutin	Pfizer <i>New York, NY</i>	MAC prophylaxis in patients with advanced HIV infection
NebuPent® aerosol pentamidine isethionate	Astellas Pharma US <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
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)
Noxafil® posaconazole	Schering-Plough <i>Kenilworth, NJ</i>	prevention of invasive fungal infections caused by <i>Aspergillus</i> and <i>Candida</i>
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)	Astellas Pharma US <i>Deerfield, IL</i>	PCP treatment

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
Priftin® rifapentine	sanofi-aventis <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 immunoabsorption	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
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
Vitrasert® Implant	Bausch & Lomb <i>Rochester, NY</i>	CMV retinitis in AIDS patients
Vitravene™ fomivirsen	Isis Pharmaceuticals <i>Carlsbad, CA</i>	CMV retinitis in AIDS patients

APPROVED MEDICINES FOR AIDS-RELATED CONDITIONS

Product Name	Company	Indication
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

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 disease 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.

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.

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.

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 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 2004 ¹	U.S. AIDS Deaths through 2004 ¹
Adults/Adolescents	934,862	523,598
Pediatric (under age 13)	9,443	5,515
TOTAL	944,305	529,113

HIV/AIDS Worldwide²

- An estimated 38.6 million people worldwide were living with HIV at the end of 2005. That year, an estimated 4.1 million people became newly infected with HIV, and an estimated 2.8 million lost their lives to AIDS.
- Africa remains the global epicenter of 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—on average, three women are HIV-positive for every two men. 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 2004)¹

- The U.S. Centers for Disease Control and Prevention (CDC) estimates that approximately 40,000 people become infected with HIV annually. In 2004, 38,730 cases of HIV/AIDS were diagnosed in the 35 areas (33 states, Guam, and the U.S. Virgin Islands) with long-term, confidential name-based HIV reporting. Almost three-fourths of HIV/AIDS diagnoses were for male adolescents and adults. The largest number of cases occurred among people ages 35-39, accounting for 17 percent of all HIV/AIDS cases diagnosed that year.
- From 2001 through 2004, the estimated number of HIV/AIDS cases increased among whites, Asians/Pacific Islanders, and American Indians/Alaska Natives, while decreasing among African Americans and Hispanics. Despite the decrease among African Americans, they accounted for half of all HIV/AIDS diagnoses in 2004.
- Through 2004, an estimated 229,411 people were reported as having HIV infection (not AIDS). By sex that year, 70 percent of the 33,132 reported cases of HIV infection (not AIDS) among adults and adolescents were in males and 30 percent were in females. In children, 431 cases of HIV infection (not AIDS) were reported.
- During the mid- to late-1990s, advances in treatment slowed the progression of HIV infection to AIDS and led to dramatic decreases in AIDS deaths. Although the decrease in the number of AIDS deaths continues (8 percent from 2000 through 2004), the number of AIDS diagnoses increased 8 percent during that period. Better treatments have also led to an increase in the number of people in the United States who are living with AIDS. From 2000 through 2004, the estimated number of people living with AIDS increased from 320,177 to 415,193—an increase of 30 percent.
- From 2000-2004, the estimated number of AIDS cases decreased 61 percent among children younger than age 13, 11 percent in the age group 30-34, and 10 percent in the age group 35-39. The largest number of AIDS cases occurred among people ages 40-44, accounting for 21 percent of all AIDS cases diagnosed in 2004. That year, 122 AIDS cases were reported in children.

* 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

Opportunistic Infections

- **AIDS-related non-Hodgkin lymphoma (NHL)** is the second most common cancer associated with HIV/AIDS after **Kaposi's sarcoma**.³ 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 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.⁴
- ***Candida albicans***, a **fungal pathogen** present in 80 percent of humans, is usually harmless or can cause mild oral and vaginal infections in otherwise healthy people. But in people whose immune systems are suppressed (such as by HIV/AIDS), it can produce deadly, systemic infections, causing death in up to 50 percent of cases. About 25,000 Americans develop these fungal infections each year, and despite treatment with antifungal drugs, 10,000 die. The number of hospital-acquired *C. albicans* infections is increasing, but there are few drugs available for treatment, and the fungus often becomes drug-resistant.⁵
- 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.⁶
- Because there is no clear definition of **lipodystrophy**, doctors report that between 5 percent and 75 percent of HIV/AIDS patients taking antiretroviral medications have some signs of the disorder. Most researchers think the true rate is about 50 percent.⁴
- ***Mycobacterium avium* complex (MAC)** disease is among the most common bacterial infections in people with HIV. In one study, MAC bacteria were found in the blood of 43 percent of people within two years of diagnosis with AIDS. MAC is most likely to occur in people with CD4+ cell counts below 50 and at least one other opportunistic infection.⁴
- Up to one-third of people with HIV may get some symptoms of **peripheral neuropathy**, which may be caused by HIV itself, medications, or both.⁷
- ***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
- Researchers estimate that HIV-positive individuals who are unaware of their infection account for 54 percent to 70 percent of new HIV infections, depending on the number of uninfected partners with whom they have unprotected sex. If all HIV-positive individuals were tested in a timely manner and reduced their high-risk sexual activity with HIV-negative partners by a little more than half, the rate of new **sexually transmitted HIV infections** could be reduced by about 30 percent a year.⁸
- The United States has the highest **sexually transmitted disease (STD)** rates of any industrialized country. (STDs include human papillomavirus [HPV], trichomoniasis, chlamydia, genital herpes, gonorrhea, **HIV**, syphilis, and hepatitis B.) More than 65 million people are currently living with an incurable STD, and some 19 million new STDs occur each year. More than half of all Americans will have an STD at some point in their lifetime.⁹

SELECTED FACTS ABOUT HIV/AIDS

Opportunistic Infections (continued)

- 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, 7,500.⁹
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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).¹⁰
 - The estimated annual cost of perinatal prevention of **HIV infection** (HIV counseling and testing and AZT treatment for infected mothers and their children) in the United States is \$67.6 million. That investment prevents 656 HIV infections and saves \$105.6 million in medical care costs alone—a net cost-savings of \$38.1 million annually.¹
 - 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.⁹
 - The direct cost associated with the 9.1 million **STD** cases among the 15- to 24-year-old age group was \$6.5 billion in year 2000 dollars. CDC researchers and economists tracked the lifetime medical cost per case of eight STDs within that age group: HIV, HPV, genital herpes simplex type 2, hepatitis B, chlamydia, gonorrhea, trichomoniasis, and syphilis. They found that HIV and HPV had the highest estimated direct medical costs at \$5.9 billion, accounting for 90 percent of the total cost. Incurable viral STDs (genital herpes, HIV, hepatitis B, and HPV) accounted for 94 percent of the total costs, while non-viral curable infections (chlamydia, gonorrhea, syphilis, and trichomoniasis) accounted for 6 percent of the total costs.⁴
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Sources:

1. U.S. Centers for Disease Control and Prevention (www.cdc.gov)
2. UNAIDS, Joint U.N. Programme on HIV/AIDS (www.unaids.org)
3. People Living with Cancer (www.plwc.org)
4. The Body: An AIDS and HIV Information Resource (www.thebody.com)
5. Science Daily (www.sciencedaily.com)
6. American Cancer Society (www.cancer.org)
7. Gay Men's Health Crisis (www.gmhc.org)
8. HIVandHepatitis.com (www.hivandhepatitis.com)
9. Guttmacher Institute (www.guttmacher.org)
10. Emory University Health Sciences Center (www.eurekaalert.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
		Phase I	Phase II	Phase III		
Years	6.5	1.5	2	3.5	1.5	
Test Population	Laboratory and animal studies	20 to 100 healthy volunteers	100 to 500 patient volunteers	1,000 to 5,000 patient volunteers	Review process/ approval	Additional post-marketing testing required by FDA
Purpose	Assess safety, biological activity and formulations	Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use		
Success Rate	5,000 compounds evaluated	5 enter trials			1 approved	

THE DRUG DEVELOPMENT AND APPROVAL PROCESS

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

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

On average, it costs a company \$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 28 new therapeutics approved by the FDA in 2005 was 12.5 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 \$39.4 billion in research and development in 2005.

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

AIDS Action Council
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 Nurses Association
American Social Health Association
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National Alliance for Hispanic Health
National Black Nurses Association
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Planned Parenthood Federation of America
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