

Alzheimer's Disease

PRESENTED BY AMERICA'S BIOPHARMACEUTICAL RESEARCH COMPANIES

Biopharmaceutical Research Companies Are Developing Nearly 100 Medicines for Alzheimer's Disease and Other Dementias

Today, more than 5 million Americans are suffering from Alzheimer's disease, robbing them of their independence and even their identity. The disease ravages the minds of patients, crushes entire families and currently costs the health care system \$172 billion a year—or 18 times more than the national cost of providing school lunches to poor children. Moreover, while huge, the figure does not include the personal costs to an estimated 11 million family members and friends who provide about 12 billion hours of unpaid care each year to those suffering from Alzheimer's.

These sobering statistics are projected to get much worse as Americans in the baby boom generation age. The first of 76 million baby boomers will turn 65 this January. Their numbers will soon swell the elderly population, and thus the number of people prone to Alzheimer's disease.

If no new medicines are found to prevent, delay or stop the progression of Alzheimer's disease, the number of afflicted in America will jump to 13.5 million by 2050, according to the Alzheimer's Association. Costs for care for Alzheimer's patients will increase five-fold to \$1.08 trillion a year. That is about 25 times more than this year's budget for the Department of Homeland Security.

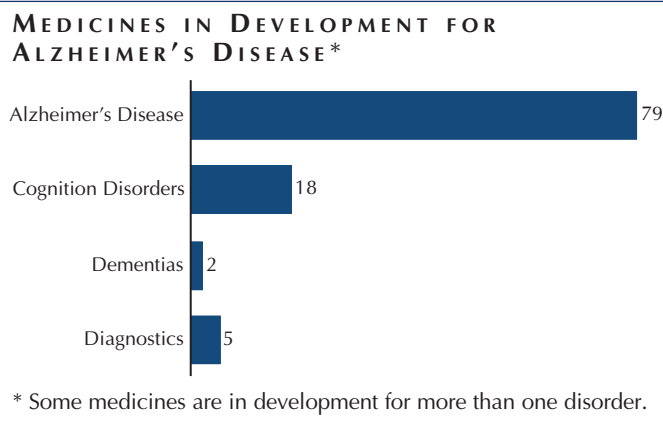
Treatments and cures have been elusive for this complicated disease. Currently, five medications on the market temporarily reduce symptoms for some, but there is no vaccine to prevent Alzheimer's or medicines to cure it or even delay onset or severity.

Hope for the future lies in medical innovation. America's biopharmaceutical companies today have 98 medicines in the later stages of the pipeline, meaning they are either in clinical trials or awaiting FDA review.

Even modest progress can drastically change the trajectory, which some warn is like a "tsunami" headed our way. For example, a breakthrough that delays the onset of Alzheimer's disease by just five years would mean a significant drop in the number of Alzheimer's patients. Instead of 13.5 million Americans suffering from the disease in 2050, the number would be 7.7—only a little more than today. Overall, a treatment to delay onset by five years would save the health care system \$447 billion.

Most importantly, such a breakthrough would reduce an untold amount of suffering for patients and their families. The implications are global, as the net balance of the world's elderly population grows by an estimated 847,000 a month.

America's biopharmaceutical researchers are exploring various new pathways to attack this devastating disease.



Examples of new approaches to treating Alzheimer's disease include:

- An oral medicine that inhibits the formation and accumulation of amyloid-beta protein deposits and may also reduce tau protein from forming neurofibrillary tangles in the brain.
- An intranasal medicine that is able to penetrate the blood-brain barrier is in development for mild cognitive impairment, a precursor to Alzheimer's disease. It has shown ability to reduce accumulation of both amyloid-beta and tau protein.
- A gene therapy for the treatment of Alzheimer's disease symptoms, such as short term memory loss, delivers a gene for nerve growth factor to the brain to prevent cell death and reverse memory loss.
- A vaccine that targets the amyloid-beta protein in the brain is designed to induce an immune response with specificity versus a systemic immune response.

The quest is intense and financially risky. Each new medicine costs, on average, more than \$1 billion and takes 10 to 15 years to develop. But new scientific advances are increasing our knowledge, and researchers are using every cutting-edge tool at their disposal. With continued dedication, we hope to make a difference for every person at risk of suffering from this terrible, debilitating disease.

Sincerely,

John J. Castellani
President and CEO
PhRMA

Medicines in Development for Alzheimer's Disease and Other Dementias

ALZHEIMER'S DISEASE AND DEMENTIAS

Product Name	Sponsor	Indication	Development Status*
18-flutemetamol (PET imaging agent)	GE Healthcare <i>Waukesha, WI</i>	Alzheimer's disease diagnosis	Phase III www.gehealthcare.com
AAB-002	Janssen Alzheimer Immunotherapy <i>South San Francisco, CA</i> Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase 0 (800) 817-5286 (860) 732-5156
AAB-003	Janssen Alzheimer Immunotherapy <i>South San Francisco, CA</i> Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase 0 completed (800) 817-5286 (860) 732-5156
AAD-2004	AmKor Pharma <i>Sammamish, WA</i> Neurotech Pharmaceuticals <i>Seoul, South Korea</i>	Alzheimer's disease	Phase I www.amkorpharma.com
ABT-126	Abbott Laboratories <i>Abbott Park, IL</i>	Alzheimer's disease	Phase II (847) 937-6100
		Alzheimer's disease in the elderly	Phase I (847) 937-6100
ABT-288	Abbott Laboratories <i>Abbott Park, IL</i>	Alzheimer's disease	Phase II (847) 937-6100
ABT-384	Abbott Laboratories <i>Abbott Park, IL</i>	Alzheimer's disease	Phase II (847) 937-6100
ABT-560	Abbott Laboratories <i>Abbott Park, IL</i>	cognition disorders	Phase I (847) 937-6100
ACC-002	Janssen Alzheimer Immunotherapy <i>South San Francisco, CA</i> Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase 0 (800) 817-5286 (860) 732-5156
AD02 vaccine	AFFiRis <i>Vienna, Austria</i> GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	Alzheimer's disease	Phase II (888) 825-5249
ADS-8703	Adamas Pharmaceuticals <i>Emeryville, CA</i>	dementia	Phase II (510) 450-3500
AMG 747	Amgen <i>Thousand Oaks, CA</i>	cognition disorders associated with schizophrenia	Phase I (805) 447-1000
ARC029 (nilvadipine)	Archer Pharmaceuticals <i>Sarasota, FL</i>	Alzheimer's disease	Phase I (941) 755-6644

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

ALZHEIMER'S DISEASE AND DEMENTIAS

Product Name	Sponsor	Indication	Development Status
ARC031	Archer Pharmaceuticals <i>Sarasota, FL</i>	Alzheimer's disease	Phase I (941) 755-6644
ARC031-SR (sustained-release)	Archer Pharmaceuticals <i>Sarasota, FL</i>	Alzheimer's disease	Phase I (941) 755-6644
ASP 0777	Astellas Pharma US <i>Deerfield, IL</i>	Alzheimer's disease	Phase I (800) 695-4321
AV965	Avera Pharmaceuticals <i>San Diego, CA</i>	Alzheimer's disease, cognition disorders	Phase I (858) 847-0650
AVN 101	Avineuro Pharmaceuticals <i>San Diego, CA</i>	Alzheimer's disease	Phase II (858) 436-1537
AVN 322	Avineuro Pharmaceuticals <i>San Diego, CA</i>	Alzheimer's disease	Phase I (858) 436-1537
AVN 397	Avineuro Pharmaceuticals <i>San Diego, CA</i>	Alzheimer's disease	Phase II (858) 436-1537
Axona™	Accera <i>Broomfield, CO</i>	age-associated memory impairment (AAMI)	Phase II (303) 439-0004
AZD1446 (TC-6683)	AstraZeneca <i>Wilmington, DE</i> Targacept <i>Winston-Salem, NC</i>	Alzheimer's disease	Phase II completed (800) 236-9933 (336) 480-2100
AZD5213	AstraZeneca <i>Wilmington, DE</i>	Alzheimer's disease	Phase I (800) 236-9933
BACE1 protein inhibitor	Ligand Pharmaceuticals <i>La Jolla, CA</i> Merck <i>Whitehouse Station, NJ</i>	Alzheimer's disease	Phase I (858) 550-7500 (800) 672-6372
BAN2401 (anti-beta amyloid antibody)	Eisai <i>Woodcliff Lake, NJ</i>	Alzheimer's disease	Phase I (888) 274-2378
bapineuzumab (AAB-001)	Janssen Alzheimer Immunotherapy <i>South San Francisco, CA</i> Pfizer <i>New York, NY</i>	Alzheimer's disease (intravenous) (Fast Track) Alzheimer's disease (subcutaneous)	Phase III (800) 817-5286 (860) 732-5156 Phase II (800) 817-5286 (860) 732-5156
BAY 85-8101 (PET imaging agent)	Bayer HealthCare Pharmaceuticals <i>Wayne, NJ</i>	Alzheimer's disease diagnosis	Phase I (888) 842-2937
BAY 94-9172 (florbetaben) (PET imaging agent)	Avid Radiopharmaceuticals <i>Philadelphia, PA</i> Bayer HealthCare Pharmaceuticals <i>Wayne, NJ</i>	Alzheimer's disease diagnosis	Phase III (215) 298-0700 (888) 842-2937
bisnorcymserine (BNC)	QR Pharma <i>Radnor, PA</i>	advanced Alzheimer's disease	Phase I (484) 253-2296
C105	Cognition Pharmaceuticals <i>New York, NY</i>	cognitive impairment/deficit associated with multiple sclerosis	Phase II (212) 906-7071

ALZHEIMER'S DISEASE AND DEMENTIAS

Product Name	Sponsor	Indication	Development Status
CAD106	Cytos Biotechnology <i>Postfach, Switzerland</i> Novartis Pharmaceuticals <i>East Hanover, NJ</i>	Alzheimer's disease	Phase II (888) 669-6682
CEP-26401	Cephalon <i>Frazer, PA</i>	cognition disorders	Phase I (610) 344-0200
CERE-110 (gene therapy)	Ceregene <i>San Diego, CA</i>	Alzheimer's disease	Phase II (858) 458-8800
CHF 5074	Chiesi Pharmaceuticals <i>Rockville, MD</i>	Alzheimer's disease	Phase I completed (301) 424-2661
CTS-21166	Astellas Pharma US <i>Deerfield, IL</i> CoMentis <i>South San Francisco, CA</i>	Alzheimer's disease	Phase I (800) 695-4321 (650) 359-2600
CX717	Cortex Pharmaceuticals <i>Irvine, CA</i>	Alzheimer's disease	Phase II (949) 727-3157
davunetide intranasal (AL-108)	Allon Therapeutics <i>Vancouver, Canada</i>	Alzheimer's disease, mild cognitive impairment	Phase II (604) 736-0634
davunetide intravenous (AL-208)	Allon Therapeutics <i>Vancouver, Canada</i>	mild cognitive impairment	Phase II (604) 736-0634
docosahexaenoic acid	Martek Biosciences <i>Columbia, MD</i>	Alzheimer's disease	Phase III (410) 740-0081
E2212 (gamma secretase inhibitor)	Eisai <i>Woodcliff Lake, NJ</i>	Alzheimer's disease	Phase I (888) 274-2378
EGb 761	Ipsen <i>Milford, MA</i>	Alzheimer's disease	Phase III (508) 478-8900
ELND005	Elan Pharmaceuticals <i>South San Francisco, CA</i> Transition Therapeutics <i>Toronto, Canada</i>	Alzheimer's disease (Fast Track)	Phase II completed (650) 877-0900 (416) 260-7770
ELND006	Elan Pharmaceuticals <i>South San Francisco, CA</i>	Alzheimer's disease	Phase I (650) 877-0900
EVP-0334	EnVivo Pharmaceuticals <i>Watertown, MA</i>	Alzheimer's disease	Phase I completed (617) 225-4250
EVP-6124	EnVivo Pharmaceuticals <i>Watertown, MA</i>	Alzheimer's disease	Phase II (617) 225-4250
Exebryl-1®	ProteoTech <i>Kirkland, WA</i>	Alzheimer's disease	Phase I (425) 823-0400
florbetapir F 18 (PET imaging agent)	Avid Radiopharmaceuticals <i>Philadelphia, PA</i>	Alzheimer's disease diagnosis	Phase III (215) 298-0700
Gammagard S/D™ immune globulin (IVIG)	Baxter Healthcare <i>Deerfield, IL</i>	early-stage Alzheimer's disease, mid-stage Alzheimer's disease	Phase III (800) 422-9837

ALZHEIMER'S DISEASE AND DEMENTIAS

Product Name	Sponsor	Indication	Development Status
gamma secretase inhibitor	Bristol-Myers Squibb <i>Princeton, NJ</i>	prodromal Alzheimer's disease	in clinical trials (212)-546-4000
gamma secretase inhibitor	Bristol-Myers Squibb <i>Princeton, NJ</i>	Alzheimer's disease	Phase II (212) 546-4000
GSK239512	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	Alzheimer's disease	Phase II (888) 825-5249
		mild cognitive impairment	Phase I completed (888) 825-5249
GSK742457	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	Alzheimer's disease	Phase II (888) 825-5249
GSK933776A	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	Alzheimer's disease	Phase I (888) 825-5249
GSK1034702	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	cognition disorders	Phase I completed (888) 825-5249
HPP-854	TransTech Pharma <i>High Point, NC</i>	Alzheimer's disease	Phase I (336) 841-0300
HT-0712	Helicon Therapeutics <i>Farmingdale, NY</i>	cognition disorders	Phase I (631) 370-8818
HTC-867	Pfizer <i>New York, NY</i>	cognitive impairment associated with schizophrenia	Phase I (860) 732-5156
huperzine A	Neuro-Hitech <i>New York, NY</i>	Alzheimer's disease	Phase II (212) 594-1225
intravenous normal human immunoglobulin	Grifols USA <i>Los Angeles, CA</i>	Alzheimer's disease	in clinical trials (888) 474-3657
latrepirdine (dimebolin)	Medivation <i>San Francisco, CA</i> Pfizer <i>New York, NY</i>	early-stage Alzheimer's disease	Phase III (415) 543-3470 (860) 732-5156
		Alzheimer's disease (combination therapy)	Phase I (415) 543-3470 (860) 732-5156
Lu AE58054	Lundbeck <i>Deerfield, IL</i>	Alzheimer's disease, psychosis or cognitive impairment associated with schizophrenia	Phase II (800) 455-1141
LY451395	Eli Lilly <i>Indianapolis, IN</i>	agitation in Alzheimer's disease	Phase II (800) 545-5979
LY2886721	Eli Lilly <i>Indianapolis, IN</i>	Alzheimer's disease	Phase I (800) 545-5979
MCD-386CR	Mithridion <i>Madison, WI</i>	Alzheimer's disease	Phase I (608) 443-2432
MK3134	Merck <i>Whitehouse Station, NJ</i>	dementia	Phase I completed (800) 672-6372
MK3328 (PET imaging agent)	Merck <i>Whitehouse Station, NJ</i>	Alzheimer's disease diagnosis	Phase I (800) 672-6372

ALZHEIMER'S DISEASE AND DEMENTIAS

Product Name	Sponsor	Indication	Development Status
NIC5-15	Humanetics <i>Eden Prairie, MN</i>	Alzheimer's disease	Phase II completed (952) 937-7660
NSA-789	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase I (860) 732-5156
Octagam® 10% immune globulin	Octapharma USA <i>Hoboken, NJ</i>	Alzheimer's disease in the elderly	Phase II (201) 604-1130
Oxigon™ indolepropionic acid derivative	Intellect Neurosciences <i>New York, NY</i>	Alzheimer's disease	Phase I completed (212) 448-9300
PF-3654746	Pfizer <i>New York, NY</i>	Alzheimer's disease (adjunctive treatment)	Phase I (860) 732-5156
PF-4360365 (ponezumab)	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase II (860) 732-5156
PF-4447943	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase II (860) 732-5156
		Alzheimer's disease (combination therapy)	Phase I (860) 732-5156
PF-4494700	Pfizer <i>New York, NY</i> TransTech Pharma <i>High Point, NC</i>	Alzheimer's disease	Phase II (860) 732-5156
PF-4995274	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase I (860) 732-5156
PF-5212365	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase II (860) 732-5156
PF-5212377	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase I (860) 732-5156
PF-5236806 (ACC-001)	Janssen Alzheimer Immunotherapy <i>South San Francisco, CA</i> Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase II (800) 934-5556 (212) 407-5740
Posiphen™ R-phenserine	QR Pharma <i>Radnor, PA</i>	Alzheimer's disease, mild cognitive impairment	Phase II (484) 253-2296
PRX-3140	Nantherapeutics <i>Alachua, FL</i>	Alzheimer's disease	Phase II (386) 462-9663
RG1450 (gantenerumab)	Roche <i>Nutley, NJ</i>	Alzheimer's disease	Phase I (973) 235-5000
RG1662	Roche <i>Nutley, NJ</i>	Alzheimer's disease	Phase I (973) 235-5000
RG3487	Roche <i>Nutley, NJ</i>	Alzheimer's disease, cognitive impairment associated with schizophrenia	Phase II (973) 235-5000
RG7412 (anti-Abeta)	AC Immune <i>Lausanne, Switzerland</i> Genentech <i>South San Francisco, CA</i>	Alzheimer's disease	Phase I (800) 626-3553

ALZHEIMER'S DISEASE AND DEMENTIAS

Product Name	Sponsor	Indication	Development Status
RVX-208	Resverlogix <i>Calgary, Canada</i>	Alzheimer's disease	Phase I (403) 254-9252
SAR110894	sanofi-aventis <i>Bridgewater, NJ</i>	Alzheimer's disease	Phase I (800) 633-1610
SEP-227900	Sepracor <i>Marlborough, MA</i>	Alzheimer's disease, cognition disorders	Phase I (508) 481-6700
solanezumab	Eli Lilly <i>Indianapolis, IN</i>	Alzheimer's disease	Phase III (800) 545-5979
ST-101	Sonexa Therapeutics <i>San Diego, CA</i>	Alzheimer's disease	Phase II (858) 356-6250
SYN-114	Synosia Therapeutics <i>South San Francisco, CA</i>	cognition disorders	Phase I (650) 244-4850
SYN-120	Synosia Therapeutics <i>South San Francisco, CA</i>	cognition disorders	Phase I (650) 244-4850
T-817MA	Toyama Chemical <i>Tokyo, Japan</i>	Alzheimer's disease	Phase II
TC-5619	AstraZeneca <i>Wilmington, DE</i> Targacept <i>Winston-Salem, NC</i>	cognition disorders associated with schizophrenia	Phase II (800) 236-9933
TD-5108	Theravance <i>South San Francisco, CA</i>	Alzheimer's disease	Phase I (877) 275-8479
TD-8954	Theravance <i>South San Francisco, CA</i>	Alzheimer's disease	Phase I (877) 275-8479
UB-311 vaccine	United Biomedical <i>Hauppauge, NY</i>	mild to moderate Alzheimer's disease	Phase I (631) 273-2828
V950 vaccine	Merck <i>Whitehouse Station, NJ</i>	Alzheimer's disease	Phase I (800) 672-6372
varenicline	Pfizer <i>New York, NY</i>	Alzheimer's disease	Phase II (860) 732-5156

The content of this report has been obtained through industry sources and the Adis "R&D Insight" database based on the latest information. **Report current as of October 8, 2010.** The information may not be comprehensive. For more specific information about a particular product, contact the individual company directly or go to www.clinicaltrials.gov. The entire series of *Medicines in Development* is available on PhRMA's web site.

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Alzheimer's disease—Progressive and chronic deterioration of all mental functions. Early manifestations include a decrease in attention span, impaired powers of concentration, some personality change and forgetfulness. As the disease progresses, there is a loss of computational ability, in addition to word-finding problems and difficulty with ordinary activities. Ultimately, there is severe memory loss, complete disorientation, social withdrawal, loss of independence, and is fatal. It is the seventh leading cause of death in the United States.

application submitted—An application for marketing has been submitted to the U.S. Food and Drug Administration (FDA). The application can either be an NDA (new drug application) or a BLA (biologic license application).

dementia—Degeneration of central nervous system functions, such as memory and learning capacity. The natural decline of these functions with age is grossly exaggerated in dementia.

Fast Track—A process designed to facilitate the development and expedite the review of drugs to treat serious diseases and fill an unmet medical need. The status is assigned by the U.S. Food and Drug Administration. The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious diseases. Generally, determining factors include whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more

serious one. Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially superior to existing therapy. Once a drug receives Fast Track designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

Lewy bodies—Abnormal protein deposits that disrupt the brain's normal functioning. In Lewy body dementia, these abnormal proteins are diffused throughout other areas of the brain, including the cerebral cortex. The brain chemical acetylcholine is depleted, causing disruption of perception, thinking and behavior. Lewy body dementia exists either in pure form, or in conjunction with other brain changes, including those typically seen in Alzheimer's disease and Parkinson's disease. Pattern of decline may be similar to Alzheimer's, including problems with memory and judgment as well as behavioral changes. Alertness and severity of cognitive symptoms may fluctuate daily. Visual hallucinations, muscle rigidity and tremors are common.

mixed dementia—Characterized by a mixture of common Alzheimer's symptoms and another dementia—most commonly vascular dementia but also other types such as Lewy dementia, which presents some symptoms similar to those of Parkinson's Disease.

mild Alzheimer's disease—As Alzheimer's disease progresses, memory loss continues, and changes in other cognitive abilities appear. Problems can include getting lost, trouble handling money and paying bills, repeating questions, taking longer to complete normal daily tasks, poor judgment, and small mood and personality changes. People often are diagnosed at this stage.

moderate Alzheimer's disease—In this stage, damage occurs in areas of the brain that control language, reasoning, sensory processing, and conscious thought. Memory loss and confusion increase, and people begin to have problems recognizing family and friends. They may be unable to learn new things, carry out tasks that involve multiple steps (such as getting dressed), or cope with new situations. They may have hallucinations, delusions, and paranoia, and may behave impulsively.

PET imaging agent—Positron emission tomography, a noninvasive imaging technique which produces three-dimensional images of the body.

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

Phase I—Safety testing and pharmacological profiling of new drugs in small numbers of humans.

GLOSSARY

Phase II—Effectiveness testing and identification of side effect profile of new drugs in humans.

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

Phase IV—Additional post-market testing of drugs sometimes required by FDA.

severe Alzheimer’s disease—By the final stage, plaques and tangles have spread throughout the brain and brain tissue has shrunk significantly. People with severe Alzheimer’s cannot communicate and are completely dependent on others for their care. Near the end, the person may be in bed most or all of the time as the body shuts down.

vascular dementia—A dementia with symptoms similar to Alzheimer’s, but memory loss may not be as great. It is caused by decreased blood flow to parts of the brain, often due to a series of small strokes, and so is also known as post-stroke dementia or vascular cognitive impairment.

SELECTED FACTS ABOUT ALZHEIMER'S DISEASE AND OTHER DEMENTIAS

Alzheimer's Disease/Dementias

- Today, 5.3 million people are living with **Alzheimer's**—every 70 seconds, someone develops the disease.
- Some 5.1 million people with Alzheimer's are age 65 and older, but an estimated 500,000 people younger than age 65 either have Alzheimer's or another **dementia**.
- **Alzheimer's disease** is the most common type of **dementia**, accounting for 60 percent to 80 percent of cases.
- **Vascular dementia** (also called multi-infarct dementia, post-stroke dementia, or vascular cognitive impairment) is considered the second most common type after Alzheimer's.
- In 2000, an estimated 411,000 new cases of **Alzheimer's** were diagnosed. That number was expected to increase to 454,000 new cases a year by 2010; 615,000 annually by 2030; and 959,000 new cases a year by 2050. By that year, the number of people age 65 and older with Alzheimer's could be as high as 13.5 million unless researchers find a way to prevent or treat the disease.
- In 2006, **Alzheimer's** was listed as the “underlying cause of death” for 72,432 Americans. In 1991, only 14,112 death certificates recorded Alzheimer's as the underlying cause. This increase could be due to reporting changes and an increase in actual Alzheimer's deaths. From 2000-2006, deaths from Alzheimer's increased by 46.1 percent, while the number one cause of death, heart disease, decreased by 11.1 percent.
- In 2006, Alzheimer's was the seventh leading cause of death for people of all ages and the fifth in people age 65 and older.
- Some 70 percent of people with **Alzheimer's** and other **dementias** live at home, where they are cared for by family and friends.
- In 2009, nearly 11 million family members and friends provided an average of 21.9 hours of unpaid care per week for a person with Alzheimer's disease or another dementia, for a total of about 12.5 billion hours of care. That year, the estimated economic value of the unpaid care was \$144 billion.
- About 60 percent of family and other unpaid caregivers of people with Alzheimer's disease and other dementias are women.
- People with **Alzheimer's** disease and other **dementias** are high users of health care, long-term care and hospice. Total payments for these types of care from all sources, including Medicare and Medicaid, are three times higher for older people with Alzheimer's and other dementias than for other older people. Based on the average per person payments from all sources for health care and long-term care services for people aged 65 and older with Alzheimer's disease and other dementias in 2004, total payments for 2010 are expected to be \$172 billion, including \$123 billion for Medicare and Medicaid.

Source:

2010 Alzheimer's Disease Facts and Figures, Alzheimer's Association, www.alz.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.

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

THE DRUG DEVELOPMENT AND APPROVAL PROCESS

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

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

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

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

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

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

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

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

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

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

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

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

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

TRACKING THE PHARMACEUTICAL AND BIOTECHNOLOGY RESEARCH PIPELINES

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

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

- **Cancer**—There are few things that cause patients more fear and uncertainty as a cancer diagnosis. Yet today—because of a steady stream of new and improved medicines and treatments—cancer can increasingly be managed and even beaten. *The 2009 report found 861 medicines in the pipeline.*
- **Heart Disease and Stroke**—Keeping up the momentum of drug discovery that has helped cut deaths from heart disease and stroke in half in the past three decades, biopharmaceutical companies are working on new medicines for these diseases. *The 2009 report found 312 medicines in the pipeline.*
- **Diabetes**—Approximately 4,110 people are diagnosed with diabetes every day. To help fight this disease, pharmaceutical and biotechnology researchers are working on new medicines to treat it and related conditions. *The 2010 report found 235 medicines in the pipeline.*
- **Mental Illnesses**—Pharmaceutical and biotechnology researchers are testing many new medicines to help the more than 450 million people worldwide who suffer from some form of mental illness. *The 2010 report found 313 medicines in the pipeline.*
- **Biotechnology**—Millions of people have already benefited from medicines and vaccines developed through biotechnology, and a new report offers hope that many more will benefit in the future. *The 2008 report found 633 medicines in the pipeline.*
- **Children**—Biopharmaceutical researchers are testing medicines to meet the special needs of children. These medicines offer hope that the significant improvements achieved in children's health over the past few decades will continue and even accelerate. *The 2010 report found 234 medicines in clinical trials.*
- **Older Americans**—The population of Americans over 65 is surging, and the pace will only increase over the coming years. As life expectancy continues to expand, older Americans face new and growing challenges to their health, productivity and independence. *The 2008 report found 1,026 medicines in the pipeline.*



New Medicines. New Hope.®

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