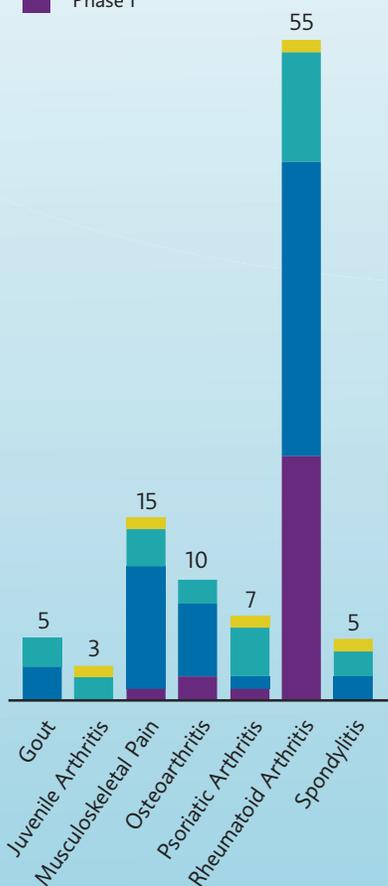


# Arthritis

A REPORT ON ARTHRITIS AND RELATED MUSCULOSKELETAL DISEASES

## Medicines in Development For Arthritis



Some medicines are listed in more than one category.

## Biopharmaceutical Research Companies Are Developing Nearly 100 Medicines for One of the Most Common Chronic Health Problems in the United States

Arthritis is part of a group of related musculoskeletal diseases consisting of more than 100 different conditions that affect more than 52 million people in the United States, according to the U.S. Centers for Disease Control and Prevention (CDC). The CDC projects prevalence of musculoskeletal diseases could increase to 67 million by 2030 if current trends continue.<sup>1</sup>

The CDC also estimates that musculoskeletal diseases cost the American economy \$128 billion annually in direct medical costs and indirect costs such as lost wages and productivity.<sup>2</sup>

Biopharmaceutical research companies are currently developing 92 medicines to help the millions of Americans affected by arthritis. These medicines are either in clinical trials or awaiting review by the U.S. Food and Drug Administration (FDA).

Of the 155 active clinical trials for arthritis medicines in the United States, 97 have not yet started recruiting patients or have just begun to seek volunteers to

participate. Another 58 are ongoing but not recruiting new patients.<sup>3</sup> The development of new, innovative therapies would not be possible without the patients who volunteer to participate in clinical trials.

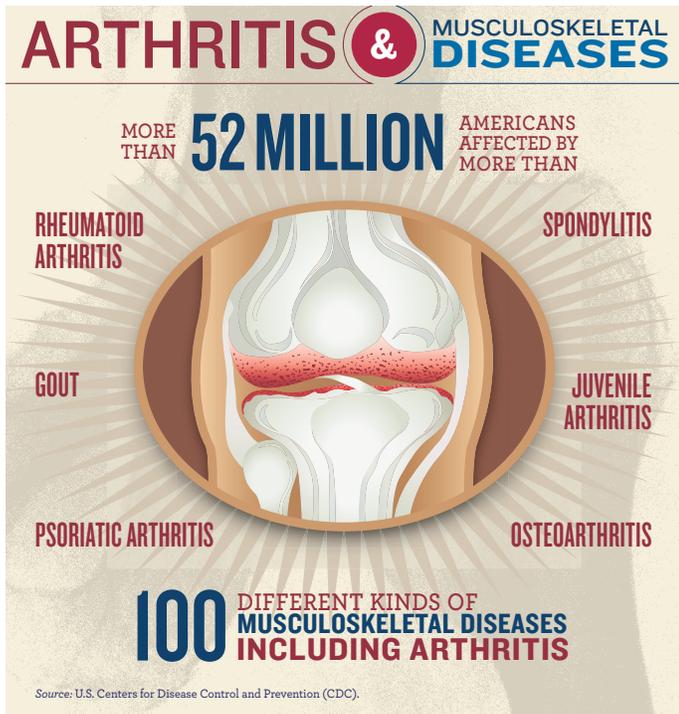
The 92 medicines in development for arthritis include:

- 55 for rheumatoid arthritis which affects an estimated 1.5 million American adults;
- 15 for musculoskeletal pain which affects the muscles, ligaments, tendons, and bones. Approximately 15 million adults report that they are unable to perform some common activities due to the pain;
- 10 for osteoarthritis, the most common form of arthritis, which affects nearly 27 million Americans; and
- 7 for psoriatic arthritis, an inflammatory arthritis, which affects approximately 30 percent of people with psoriasis.

<sup>1</sup> 2003 National Health Interview Survey, CDC

<sup>2</sup> 2003 Medical Expenditure Survey, CDC

<sup>3</sup> Source: [www.clinicaltrials.gov](http://www.clinicaltrials.gov), search performed 7/14/2014. Search criteria: arthritis, United States, Phase 0, 1, 2, 3; industry only.



Researching and developing new medicines remains a risky investment and lengthy process. On average, it costs \$1.2 billion and between 10–15 years to bring a new medicine to patients. Despite that risk, America’s biopharmaceutical research companies continue to conduct the cutting-edge research needed to reduce the destructive toll of arthritis and related musculoskeletal diseases.

## Medicines in the Pipeline

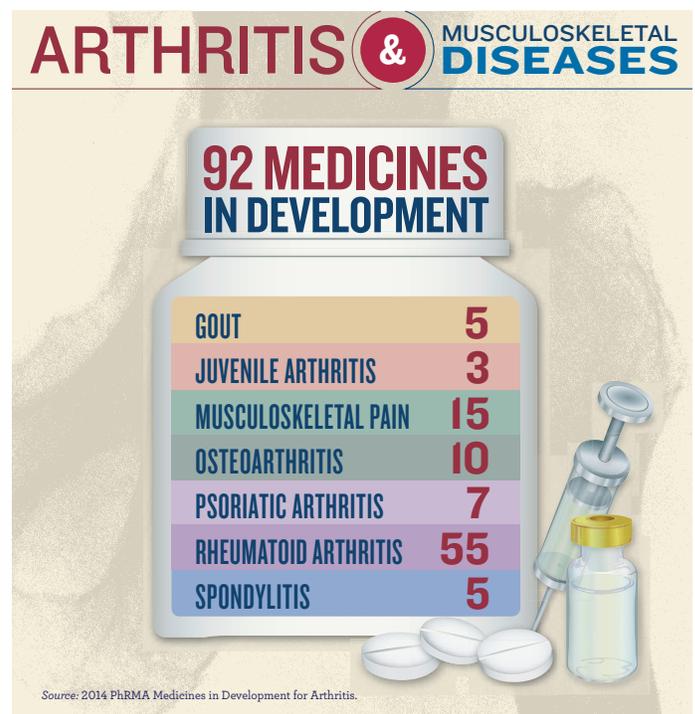
America’s biopharmaceutical research companies are exploring many different approaches to treat musculoskeletal diseases. Among the 92 innovative medicines in development for arthritis are potential treatments for:

**Ankylosing spondylitis** is a type of arthritis that most often causes inflammation in the bones and joints of the spine, but can also affect other areas. Over time, the joints become swollen and inflamed, and can fuse together. One medicine in development for ankylosing spondylitis is a human monoclonal antibody that selectively binds to and neutralizes the pro-inflammatory cytokine interleukin-17A, which causes inflammation and affects bone biology. Researchers believe it plays a role in several forms of arthritis.

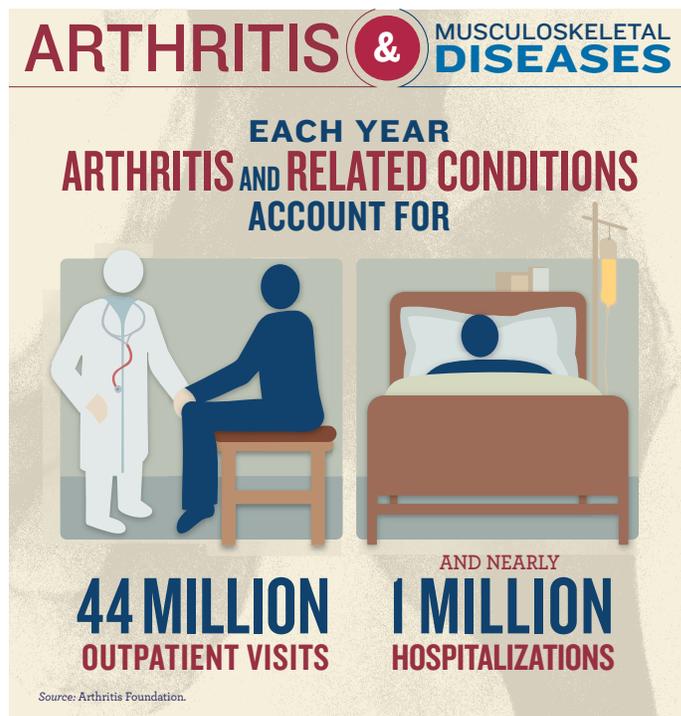
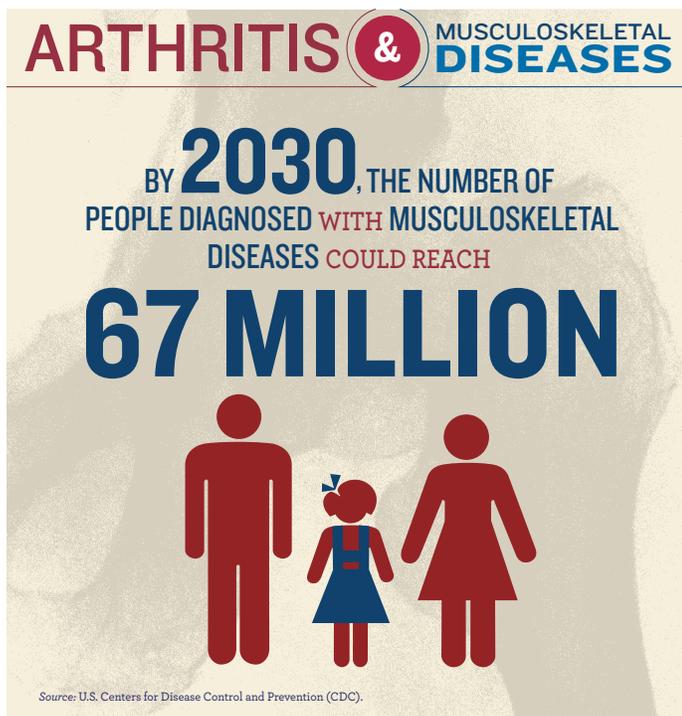
**Osteoarthritis** is the most common joint disorder, resulting from aging and wear and tear on a joint. When the cartilage breaks down and wears away, the bones rub together, causing pain, swelling, and stiffness. A medicine in development for osteoarthritis combines the function and specificity of two monoclonal antibodies into one molecular entity in order to target two different pro-inflammatory cytokines—interleukin-1 alpha and interleukin-1 beta.

**Psoriatic arthritis** is a chronic autoimmune disease that occurs in a subset of individuals who have psoriasis and causes joint pain, stiffness and swelling. A medicine in development for psoriatic arthritis is a human monoclonal antibody that binds to the interleukin-17 (IL-17) receptor. When the medicine attaches to the receptor, it prevents members of the IL-17 family from activating the receptor and exerting their full effect on the body, leading to possible inflammation.

**Rheumatoid arthritis** is a progressive, systemic autoimmune disease characterized by inflammation and swelling of the membrane lining the joints, leading to destruction of the joint. A medicine in development for rheumatoid arthritis inhibits two types of an enzyme (Janus kinase 1 and 2) that may play a role in rheumatoid arthritis. Another medicine in development for rheumatoid arthritis is



a monoclonal antibody that targets the alpha receptor of granulocyte-macrophage colony stimulating factor (GM-CSF), a key factor in the inflammatory process of rheumatoid arthritis.



### ACCELERATING MEDICINES PARTNERSHIP PILOT PROGRAM SEEKS TO ADVANCE RESEARCH ON RHEUMATOID ARTHRITIS

*The Accelerating Medicines Partnership (AMP) is a groundbreaking partnership between the National Institutes of Health, several non-profit disease foundations, 10 biopharmaceutical companies and PhRMA which began in 2014. The goal of the initiative is to transform the current model for developing new diagnostics and treatments by joining forces to identify and validate promising biological targets of disease.*

*AMP represents a new, integrated approach to treatment discovery and seeks to increase the number of new diagnostics and therapies for patients while reducing the time and cost associated with their development. The initiative will begin with three pilot projects focused on the autoimmune diseases of rheumatoid arthritis and systemic lupus erythematosus, Alzheimer's and type 2 diabetes. AMP data and analyses will be publicly accessible to the biomedical community.*

## Improving Quality of Life for Rheumatoid Arthritis Patients

Disease-modifying biological medicines have ushered in a new age of treatment for rheumatoid arthritis. By targeting the cells involved in the progression of rheumatoid arthritis, these medicines have dramatically slowed or even reversed the negative physical effects associated with the disease and made clinical remission possible for patients with severe disease. A 2010 study published in the *Journal of Rheumatology* found patients treated with combination therapy consisting of a new biologic and an older medicine had a 35 percent chance of complete clinical remission over the course of five years, compared with 14 percent for those taking only the older medicine—more than doubling remission rates for patients.

**ARTHRTIS & MUSCULOSKELETAL DISEASES**

### Improved Quality of Life...

**THEN**

Treatments reduced joint inflammation but not progression to disability

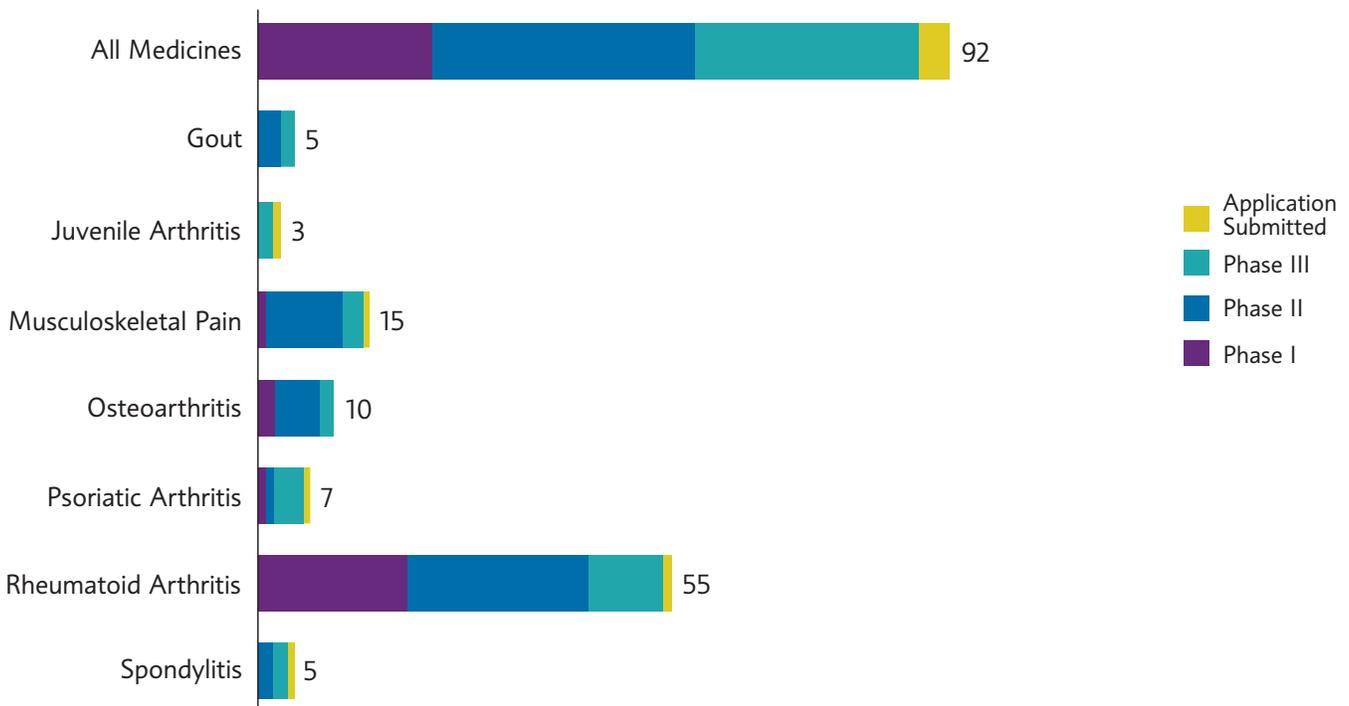
**NOW**

**DISEASE-MODIFYING ANTIRHEUMATIC DRUGS** target inflammation sources enabling disease remission

Source: C. Augustyn, B. Walker, and T.F. Goss. "Recognizing the Value of Innovation in the Treatment of Rheumatoid Arthritis." Boston, MA: Healthcare Associates, March 2013.

## Medicines in Development By Disease and Phase

Some medicines are listed in more than one category.



## Facts About Arthritis and Related Musculoskeletal Diseases

### Overview

- **Arthritis** is part of a group of related musculoskeletal diseases consisting of more than 100 different conditions that affect people of all ages, races and genders.<sup>1</sup>
- Of the estimated 52.5 million Americans with some form of **arthritis**, more than 4.6 million are African-Americans and 2.9 million are Hispanic.<sup>2</sup>
- **Arthritis** is not just a disease of old age. About 40 percent of people with arthritis are under the age of 65, including approximately 294,000 children.<sup>2</sup>
- **Arthritis and related musculoskeletal diseases** cost the U.S. economy nearly \$128 billion per year in medical care and indirect expenses, including lost wages and productivity.<sup>2</sup>

### Gout

- **Gout**, a complex form of arthritis causing sudden, severe attacks of pain, redness and tenderness in joints, occurs more often in men than in women. Men also are more likely to develop gout earlier—usually between the ages of 40 and 50—whereas women generally develop signs and symptoms after menopause.<sup>3</sup>
- A 2011 study shows the prevalence of **gout** in the United States has risen over the last twenty years and now affects 8.3 million Americans.<sup>4</sup>

### Juvenile Arthritis

- **Juvenile arthritis** refers to any form of arthritis or related condition that develops in children or teenagers who are younger than age 18. Approximately 294,000 children are affected by juvenile arthritis and rheumatologic conditions, making it one of the most common childhood diseases in the United States.<sup>1</sup>

### Musculoskeletal Pain

- Musculoskeletal diseases are a major cause of **pain** and reduced quality of life. Nearly 15 million adults report that they are unable to perform at least one common activity, such as self-care, walking, or rising from a chair, on a regular basis due to their musculoskeletal condition.<sup>5</sup>

### Osteoarthritis

- **Osteoarthritis** is a chronic condition and one of the most common forms of arthritis, affecting approximately 27 million people in the United States. Common risk factors include increasing age, obesity, previous joint injury, overuse of the joint, weak thigh muscles, and genetics.<sup>2</sup>
- Nearly 50 percent of people by the age of 85 will develop symptomatic **knee osteoarthritis**.<sup>2</sup>

### Psoriatic Arthritis

- The incidence of **psoriatic arthritis** in the United States is estimated to be 6-7 people per 100,000 population annually. The disease prevalence is approximately up to 0.1 percent of the U.S. adult population. Peak incidence occurs between the ages of 30-55, and both sexes are equally affected.<sup>6</sup>
- Up to 30 percent of people with psoriasis also develop **psoriatic arthritis**. In 85 percent of those people, psoriasis on the skin preceded arthritis joint disease.<sup>7</sup>

### Rheumatoid Arthritis

- About 1.5 million people in the United States have **rheumatoid arthritis**.<sup>2</sup> Nearly three times as many women have the disease as men. In women, rheumatoid arthritis most commonly begins between the ages of 30 and 60, whereas in men it often occurs later in life.<sup>1</sup>

### Spondylitis

- Unlike other forms of arthritis and rheumatic diseases, the general onset of **ankylosing spondylitis** commonly occurs in younger people between the ages of 17-45. However, it also can affect children and those who are much older. Ankylosing spondylitis is more common in men, but it occurs in women as well.<sup>8</sup>
- About 2.7 million American adults are estimated to have **axial spondyloarthritis**.<sup>2</sup>

### Sources:

1. Arthritis Foundation, [www.arthritis.org](http://www.arthritis.org)
2. U.S. Centers for Disease Control and Prevention, [www.cdc.gov](http://www.cdc.gov)
3. Mayo Clinic, [www.mayoclinic.org](http://www.mayoclinic.org)
4. American College of Rheumatology, [www.rheumatology.org](http://www.rheumatology.org)
5. The Burden of Musculoskeletal Diseases, United States Bone and Joint Initiative, [www.boneandjointburden.org](http://www.boneandjointburden.org)
6. Johns Hopkins Arthritis Center, [www.hopkinsarthritis.org](http://www.hopkinsarthritis.org)
7. National Psoriasis Foundation, [www.psoriasis.org](http://www.psoriasis.org)
8. Spondylitis Association of America, [www.spondylitis.org](http://www.spondylitis.org)

# Medicines in Development for Arthritis

## Gout

Product Name	Sponsor	Indication	Development Phase*
arhalofenat	CymaBay Therapeutics <i>Newark, CA</i>	gout	Phase II <a href="http://www.cymabay.com">www.cymabay.com</a>
febuxostat extended release	Takeda Pharmaceuticals <i>Deerfield, IL</i>	gout	Phase III <a href="http://www.takeda.com">www.takeda.com</a>
lesinurad (selective uric acid reabsorption inhibitor)	AstraZeneca <i>Wilmington, DE</i>	gout (chronic treatment)	Phase III <a href="http://www.astrazeneca.com">www.astrazeneca.com</a>
RDEA3170 (selective uric acid reabsorption inhibitor)	AstraZeneca <i>Wilmington, DE</i>	chronic management of hyperuricemia in patients with gout	Phase II <a href="http://www.astrazeneca.com">www.astrazeneca.com</a>
ulodesine (PNP inhibitor)	BioCryst Pharmaceuticals <i>Durham, NC</i>	gout	Phase II completed <a href="http://www.biocryst.com">www.biocryst.com</a>

## Juvenile Arthritis

Product Name	Sponsor	Indication	Development Phase
<b>Cimzia</b> <sup>®</sup> certolizumab pegol	UCB <i>Smyrna, GA</i>	juvenile idiopathic arthritis (see also rheumatoid arthritis, spondylitis)	Phase III <a href="http://www.ucb.com">www.ucb.com</a>
<b>Rasuvo</b> <sup>™</sup> methotrexate subcutaneous auto-injection	Medac Pharma <i>Chicago, IL</i>	polyarticular-course juvenile rheumatoid arthritis (see also rheumatoid arthritis)	application submitted <a href="http://www.medacpharma.com">www.medacpharma.com</a>
<b>Simponi</b> <sup>®</sup> golimumab	Janssen Biotech <i>Horsham, PA</i>	juvenile idiopathic arthritis	Phase III <a href="http://www.janssenbiotech.com">www.janssenbiotech.com</a>

\*For more information about a specific medicine or company in the report, please use the website provided.

## Musculoskeletal Pain

While musculoskeletal pain is not a type of arthritis, it is included here as an important aspect of the disease.

Product Name	Sponsor	Indication	Development Phase
AF-219 (purinoceptor P2X3 antagonist)	Afferent Pharmaceuticals <i>San Mateo, CA</i>	osteoarthritis pain	Phase II <a href="http://www.afferentpharma.com">www.afferentpharma.com</a>
<b>BEMA™</b> buprenorphine transmucosal	Endo Pharmaceuticals <i>Malvern, PA</i>	osteoarthritis pain	Phase III <a href="http://www.endo.com">www.endo.com</a>
<b>Botox®</b> onabotulinum toxin A	Allergan <i>Irvine, CA</i>	osteoarthritis pain	Phase II <a href="http://www.allergan.com">www.allergan.com</a>
cebranopadol (GRT6005)	Actavis <i>New York, NY</i> Grünenthal <i>Aachen, Germany</i>	osteoarthritis pain of the knee	Phase II completed <a href="http://www.actavis.com">www.actavis.com</a>
EP4-R antagonist	Eli Lilly <i>Indianapolis, IN</i>	osteoarthritis pain	Phase I <a href="http://www.lilly.com">www.lilly.com</a>
FX005 (sustained release p38 inhibitor)	Flexion Therapeutics <i>Burlington, MA</i>	end-stage osteoarthritis pain	Phase II completed <a href="http://www.flexiontherapeutics.com">www.flexiontherapeutics.com</a>
FX006 (sustained release steroid)	Flexion Therapeutics <i>Burlington, MA</i>	moderate to severe osteoarthritis pain	Phase II <a href="http://www.flexiontherapeutics.com">www.flexiontherapeutics.com</a>
NKTR-181 (mu-opioid analgesic)	Nektar Therapeutics <i>San Francisco, CA</i>	osteoarthritis pain of the knee	Phase II completed <a href="http://www.nektar.com">www.nektar.com</a>
OLT1177 gel	Olatec Industries <i>Rye Brook, NY</i>	moderate to severe osteoarthritis pain of the knee	Phase II
<b>SoluMatrix® Meloxicam</b> nanoparticle paroduct	Iroko Pharmaceuticals <i>Philadelphia, PA</i>	osteoarthritis pain	Phase III <a href="http://www.iroko.com">www.iroko.com</a>
<b>SoluMatrix® Naproxen</b> nanoparticle paroduct	Iroko Pharmaceuticals <i>Philadelphia, PA</i>	osteoarthritis pain	Phase II <a href="http://www.iroko.com">www.iroko.com</a>
<b>SYNVISC-ONE®</b>	Sanofi US <i>Bridgewater, NJ</i>	osteoarthritis pain of the hip	Phase III <a href="http://www.sanofi.com">www.sanofi.com</a>
TV-45070 (sodium channel inhibitor)	Teva Pharmaceutical <i>Petach Tikvah, Israel</i> Xenon Pharmaceuticals <i>Burnaby, Canada</i>	osteoarthritis pain	Phase II <a href="http://www.tevapharm.com">www.tevapharm.com</a> <a href="http://www.xenon-pharma.com">www.xenon-pharma.com</a>
V116517	Purdue Pharma <i>Stamford, CT</i>	osteoarthritis pain of the knee	Phase II completed <a href="http://www.purduepharma.com">www.purduepharma.com</a>

## Musculoskeletal Pain

Product Name	Sponsor	Indication	Development Phase
<b>Zorvolex™</b> diclofenac	Iroko Pharmaceuticals <i>Philadelphia, PA</i>	osteoarthritis pain	application submitted <a href="http://www.iroko.com">www.iroko.com</a>

## Osteoarthritis

Product Name	Sponsor	Indication	Development Phase
ABT-981 (IL-1 alpha/IL-1 beta inhibitor)	AbbVie <i>North Chicago, IL</i>	osteoarthritis of the knee	Phase II <a href="http://www.abbvie.com">www.abbvie.com</a>
<b>Ampion™</b>	Ampio Pharmaceuticals <i>Greenwood Village, CO</i>	osteoarthritis of the knee	Phase III <a href="http://www.ampiopharma.com">www.ampiopharma.com</a>
BI 1026706	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	osteoarthritis	Phase I <a href="http://www.boehringer-ingelheim.com">www.boehringer-ingelheim.com</a>
<b>Cartistem®</b> mesenchymal stem cell therapy for cartilage repair	Medipost <i>Seoul, South Korea</i>	osteoarthritis	Phase I/II <a href="http://www.medi-post.com">www.medi-post.com</a>
gevokizumab	XOMA <i>Berkeley, CA</i>	erosive osteoarthritis of the hand	Phase II <a href="http://www.xoma.com">www.xoma.com</a>
ibuprofenamine (X0002)	Techfields Pharma <i>Jiangsu, China</i>	osteoarthritis of the knee	Phase II <a href="http://www.tfpharma.com">www.tfpharma.com</a>
SM-04690 (Wnt signaling pathway modulator)	Samumed <i>San Diego, CA</i>	osteoarthritis of the knee	Phase I <a href="http://www.samumed.com">www.samumed.com</a>
sprifermin (FGF-18)	EMD Serono <i>Rockland, MA</i>	osteoarthritis	Phase II <a href="http://www.emdserono.com">www.emdserono.com</a>
TG-C (cell therapy)	TissueGene <i>Rockville, MD</i>	osteoarthritis of the knee	Phase II <a href="http://www.tissuegene.com">www.tissuegene.com</a>
TPX-100 (MEPE-derived 23-amino acid peptide)	OrthoTrophix <i>Oakland, CA</i>	osteoarthritis of the knee	Phase II <a href="http://www.orthotrophix.com">www.orthotrophix.com</a>

## Psoriatic Arthritis

Product Name	Sponsor	Indication	Development Phase
brodalumab (anti-IL-17R mAb)	Amgen <i>Thousand Oaks, CA</i> AstraZeneca <i>Wilmington, DE</i>	psoriatic arthritis	Phase III <a href="http://www.amgen.com">www.amgen.com</a> <a href="http://www.astrazeneca.com">www.astrazeneca.com</a>
clazakizumab (BMS-945429)	Bristol-Myers Squibb <i>Princeton, NJ</i>	psoriatic arthritis (see also rheumatoid arthritis)	Phase II <a href="http://www.bms.com">www.bms.com</a>
ixekizumab (IL-17 inhibitor)	Eli Lilly <i>Indianapolis, IN</i>	psoriatic arthritis	Phase III <a href="http://www.lilly.com">www.lilly.com</a>
<b>Orencia</b> <sup>®</sup> abatacept (subcutaneous)	Bristol-Myers Squibb <i>Princeton, NJ</i>	psoriatic arthritis	Phase III <a href="http://www.bms.com">www.bms.com</a>
secukinumab (IL-17 inhibitor)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	psoriatic arthritis (see also rheumatoid arthritis, spondylitis)	application submitted <a href="http://www.novartis.com">www.novartis.com</a>
ShK-186 (Kv1.3 potassium channel blocker)	Kineta <i>Seattle, WA</i>	psoriatic arthritis	Phase I <a href="http://www.kinetabio.com">www.kinetabio.com</a>
<b>Xeljanz</b> <sup>®</sup> tofacitinib	Pfizer <i>New York, NY</i>	psoriatic arthritis (see also spondylitis)	Phase III <a href="http://www.pfizer.com">www.pfizer.com</a>

## Rheumatoid Arthritis

Product Name	Sponsor	Indication	Development Phase
ABP 501 (adalimumab biosimilar)	Amgen <i>Thousand Oaks, CA</i>	rheumatoid arthritis	Phase III <a href="http://www.amgen.com">www.amgen.com</a>
ABT-122 (IL-17/TNF inhibitor)	AbbVie <i>North Chicago, IL</i>	rheumatoid arthritis	Phase I <a href="http://www.abbvie.com">www.abbvie.com</a>
ABT-494 (JAK1/JAK2/JAK3 inhibitor)	AbbVie <i>North Chicago, IL</i>	rheumatoid arthritis	Phase II <a href="http://www.abbvie.com">www.abbvie.com</a>
allogeneic mesenchymal precursor cells	Mesoblast <i>New York, NY</i>	rheumatoid arthritis	Phase II <a href="http://www.mesoblast.com">www.mesoblast.com</a>

## Rheumatoid Arthritis

Product Name	Sponsor	Indication	Development Phase
ALX-0061 (IL-6 receptor modulator)	AbbVie <i>North Chicago, IL</i> Ablynx <i>Ghent, Belgium</i>	rheumatoid arthritis	Phase I/II <a href="http://www.abbvie.com">www.abbvie.com</a> <a href="http://www.ablynx.com">www.ablynx.com</a>
ASP015K (JAK3 inhibitor)	Astellas Pharma <i>Tokyo, Japan</i> Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase II <a href="http://www.astellas.com">www.astellas.com</a> <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
baricitinib (JAK1/JAK2 inhibitor)	Eli Lilly <i>Indianapolis, IN</i> Incyte <i>Wilmington, DE</i>	rheumatoid arthritis	Phase III <a href="http://www.lilly.com">www.lilly.com</a> <a href="http://www.incyte.com">www.incyte.com</a>
BI 655064 (CD40 antigen inhibitor)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	rheumatoid arthritis	Phase I <a href="http://www.boehringer-ingelheim.com">www.boehringer-ingelheim.com</a>
BI 695500 (rituximab biosimilar)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	rheumatoid arthritis	Phase III <a href="http://www.boehringer-ingelheim.com">www.boehringer-ingelheim.com</a>
BI 695501 (adalimumab biosimilar)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	rheumatoid arthritis	Phase I <a href="http://www.boehringer-ingelheim.com">www.boehringer-ingelheim.com</a>
BT-016 (tregalizumab)	AbbVie <i>North Chicago, IL</i>	rheumatoid arthritis	Phase II <a href="http://www.abbvie.com">www.abbvie.com</a>
Btk inhibitor	Pharmacyclics <i>Sunnyvale, CA</i>	rheumatoid arthritis	Phase I <a href="http://www.pharmacyclics.com">www.pharmacyclics.com</a>
Cadherin-11 (SDP051)	Adheron Therapeutics <i>Berkeley, CA</i>	rheumatoid arthritis	Phase I completed <a href="http://www.adherontherapeutics.com">www.adherontherapeutics.com</a>
CC-292 (Btk inhibitor)	Celgene <i>Summit, NJ</i>	rheumatoid arthritis	Phase II <a href="http://www.celgene.com">www.celgene.com</a>
CCX354 (CCR1 chemokine receptor)	ChemoCentryx <i>Mountain View, CA</i>	rheumatoid arthritis	Phase I <a href="http://www.chemocentryx.com">www.chemocentryx.com</a>
CF101 (adenosine A3 receptor agonist)	Can-Fite BioPharma <i>Waltham, MA</i>	rheumatoid arthritis	Phase II <a href="http://www.canfite.com">www.canfite.com</a>
CFZ533	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	rheumatoid arthritis	Phase I <a href="http://www.novartis.com">www.novartis.com</a>
CHS-0214 (etanercept biosimilar)	Coherus Biosciences <i>Redwood City, CA</i>	rheumatoid arthritis	Phase III <a href="http://www.coherus.com">www.coherus.com</a>

## Rheumatoid Arthritis

Product Name	Sponsor	Indication	Development Phase
<b>Cimzia®</b> certolizumab pegol	UCB <i>Smyrna, GA</i>	early active rheumatoid arthritis (see also juvenile arthritis, spondylitis)	Phase III <a href="http://www.ucb.com">www.ucb.com</a>
clazakizumab (BMS-945429)	Bristol-Myers Squibb <i>Princeton, NJ</i>	rheumatoid arthritis (see also psoriatic arthritis)	Phase II <a href="http://www.bms.com">www.bms.com</a>
CNTO 6785 (IL-17A modulator)	Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase II <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
<b>Dekavil</b> F8 antibody-IL-10	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase I <a href="http://www.pfizer.com">www.pfizer.com</a>
FPA008 (IL-34/CSF1 inhibitor)	Five Prime Therapeutics <i>South San Francisco, CA</i>	rheumatoid arthritis	Phase I <a href="http://www.fiveprime.com">www.fiveprime.com</a>
GLPG0634 (JAK1 inhibitor)	AbbVie <i>North Chicago, IL</i> <i>Galapagos</i> <i>Mechelen, Belgium</i>	rheumatoid arthritis	Phase II <a href="http://www.abbvie.com">www.abbvie.com</a> <a href="http://www.glp.com">www.glp.com</a>
GSK3117391 (macrophage targeted histone deacetylase inhibitor)	GlaxoSmithKline <i>Research Triangle Park, NC</i>	rheumatoid arthritis	Phase I <a href="http://www.gsk.com">www.gsk.com</a>
GSK3196165 (MOR103) (granulocyte macrophage colony-stimulating factor mAb)	GlaxoSmithKline <i>Research Triangle Park, NC</i>	rheumatoid arthritis	Phase II <a href="http://www.gsk.com">www.gsk.com</a>
guselkumab (CNTO 1959)	Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase II completed <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
INCB47986 (JAK1 inhibitor)	Incyte <i>Wilmington, DE</i>	rheumatoid arthritis	Phase I <a href="http://www.incyte.com">www.incyte.com</a>
IPI-145 (dual PI3K inhibitor)	Infinity Pharmaceuticals <i>Cambridge, MA</i>	rheumatoid arthritis	Phase II <a href="http://www.infi.com">www.infi.com</a>
JNJ-38518168 (histamine H4 receptor antagonist)	Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase II <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
JNJ-40346527 (FMS inhibitor)	Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase II completed <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
KD025 (ROCK2 inhibitor)	Kadmon <i>New York, NY</i>	rheumatoid arthritis	Phase I <a href="http://www.kadmon.com">www.kadmon.com</a>

## Rheumatoid Arthritis

Product Name	Sponsor	Indication	Development Phase
(L/D)-aminopterin	Syntrix Biosystems <i>Auburn, WA</i>	rheumatoid arthritis	Phase II <a href="http://www.syntrixbio.com">www.syntrixbio.com</a>
LY3090106	Eli Lilly <i>Indianapolis, IN</i>	rheumatoid arthritis	Phase I <a href="http://www.lilly.com">www.lilly.com</a>
mavrilimumab (anti-GM-CSFR mAb)	MedImmune <i>Gaithersburg, MD</i>	rheumatoid arthritis	Phase II <a href="http://www.medimmune.com">www.medimmune.com</a>
MK-8808 (rituximab biosimilar)	Merck <i>Whitehouse Station, NJ</i>	rheumatoid arthritis	Phase I <a href="http://www.merck.com">www.merck.com</a>
MORAb-022 (IgG1 mAb)	Eisai <i>Woodcliff Lake, NJ</i>	rheumatoid arthritis	Phase I <a href="http://www.eisai.com">www.eisai.com</a>
NN8210 (anti-C5aR-215)	Novo Nordisk <i>Plainsboro, NJ</i>	rheumatoid arthritis	Phase I <a href="http://www.novonordisk.com">www.novonordisk.com</a>
NN8226 (anti-IL20 antibody)	Novo Nordisk <i>Plainsboro, NJ</i>	rheumatoid arthritis	Phase II <a href="http://www.novonordisk.com">www.novonordisk.com</a>
<b>Otezla</b> <sup>®</sup> apremilast	Celgene <i>Summit, NJ</i>	rheumatoid arthritis (see also spondylitis)	Phase II <a href="http://www.celgene.com">www.celgene.com</a>
PF-04171327 (selective glucocorticoid receptor modulator)	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase II <a href="http://www.pfizer.com">www.pfizer.com</a>
PF-05280586 (rituximab biosimilar)	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase I <a href="http://www.pfizer.com">www.pfizer.com</a>
PF-06410293 (adalimumab biosimilar)	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase I <a href="http://www.pfizer.com">www.pfizer.com</a>
PF-06438179 (infliximab biosimilar)	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase I <a href="http://www.pfizer.com">www.pfizer.com</a>
PRTX-100 (staphylococcal protein A)	Protalex <i>Florham Park, NJ</i>	active rheumatoid arthritis	Phase I <a href="http://www.protalex.com">www.protalex.com</a>
QAL964	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	rheumatoid arthritis	Phase II <a href="http://www.novartis.com">www.novartis.com</a>

## Rheumatoid Arthritis

Product Name	Sponsor	Indication	Development Phase
<b>Rasuvo™</b> methotrexate subcutaneous auto-injection pen	Medac Pharma <i>Chicago, IL</i>	rheumatoid arthritis (see also juvenile arthritis)	application submitted <a href="http://www.medacpharma.com">www.medacpharma.com</a>
<b>Ravax™</b> rheumatoid arthritis vaccine	Immune Response BioPharma <i>Atlantic City, NJ</i>	rheumatoid arthritis	Phase III <a href="http://www.immuneresponsebiopharma.com">www.immuneresponsebiopharma.com</a>
SAN-300 (VLA-1 mAb)	Salix Pharmaceuticals <i>Raleigh, NC</i>	rheumatoid arthritis	Phase II <a href="http://www.salix.com">www.salix.com</a>
sarilumab (anti-IL-6R mAb)	Regeneron Pharmaceuticals <i>Tarrytown, NY</i> Sanofi US <i>Bridgewater, NJ</i>	rheumatoid arthritis	Phase III <a href="http://www.regeneron.com">www.regeneron.com</a> <a href="http://www.sanofi.com">www.sanofi.com</a>
secukinumab (IL-17 inhibitor)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	rheumatoid arthritis (see also psoriatic arthritis, spondylitis)	Phase III <a href="http://www.novartis.com">www.novartis.com</a>
sirukumab (IL-6 mAb)	Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase III <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
<b>Stelara®</b> ustekinumab	Janssen Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase II completed <a href="http://www.janssenrnd.com">www.janssenrnd.com</a>
VX-509 (JAK3 inhibitor)	Vertex Pharmaceuticals <i>Boston, MA</i>	rheumatoid arthritis	Phase II <a href="http://www.vrtx.com">www.vrtx.com</a>
<b>XmAb® 5871</b> anti-CD19 mAb	Xencor <i>Monrovia, CA</i>	moderate to severe rheumatoid arthritis	Phase II <a href="http://www.xencor.com">www.xencor.com</a>

## Spondylitis

Product Name	Sponsor	Indication	Development Phase
BI 655066 (IL-23 subunit p19 inhibitor)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	ankylosing spondylitis	Phase II <a href="http://www.boehringer-ingelheim.com">www.boehringer-ingelheim.com</a>
<b>Cimzia®</b> certolizumab pegol	UCB <i>Smyrna, GA</i>	axial spondyloarthritis (see also juvenile arthritis, rheumatoid arthritis)	application submitted <a href="http://www.ucb.com">www.ucb.com</a>

## Spondylitis

Product Name	Sponsor	Indication	Development Phase
<b>Otezla®</b> apremilast	Celgene Summit, NJ	ankylosing spondylitis (see also rheumatoid arthritis)	Phase III www.celgene.com
secukinumab (IL-17 inhibitor)	Novartis Pharmaceuticals East Hanover, NJ	ankylosing spondylitis (see also psoriatic arthritis, rheumatoid arthritis)	Phase III www.novartis.com
<b>Xeljanz®</b> tofacitinib	Pfizer New York, NY	ankylosing spondylitis (see also psoriatic arthritis)	Phase II www.pfizer.com

### Definitions

**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).

**Phase I**—Researchers test the drug in a small group of people, usually between 20 and 100 healthy adult volunteers, to evaluate its initial safety and tolerability profile, determine a safe dosage range, and identify potential side effects.

**Phase II**—The drug is given to volunteer patients, usually between 100 and 500, to determine whether the drug is effective, identify an optimal dose, and to evaluate further its short-term safety.

**Phase III**—The drug is given to a larger, more diverse patient population, often involving between 1,000 and 5,000 patients (but sometimes many more thousands), to generate statistically significant evidence to confirm its safety and effectiveness. Phase III studies are the longest studies and usually take place in multiple sites around the world.

*The content of this report has been obtained through public, government and industry sources, and the Adis "R&D Insight" database based on the latest information. Report current as of July 14, 2014. The medicines in this report include medicines being developed by U.S.-based companies conducting trials in the United States and abroad, PhRMA-member companies conducting trials in the United States and abroad, and foreign companies conducting clinical trials in the United States. The information in this report may not be comprehensive. For more specific information about a particular product, contact the individual company directly or go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov). The entire series of Medicines in Development is available on PhRMA's website.*

**A publication of PhRMA's Communications & Public Affairs Department (202) 835-3460**

[www.phrma.org](http://www.phrma.org) | [www.innovation.org](http://www.innovation.org) | [www.pparx.org](http://www.pparx.org)

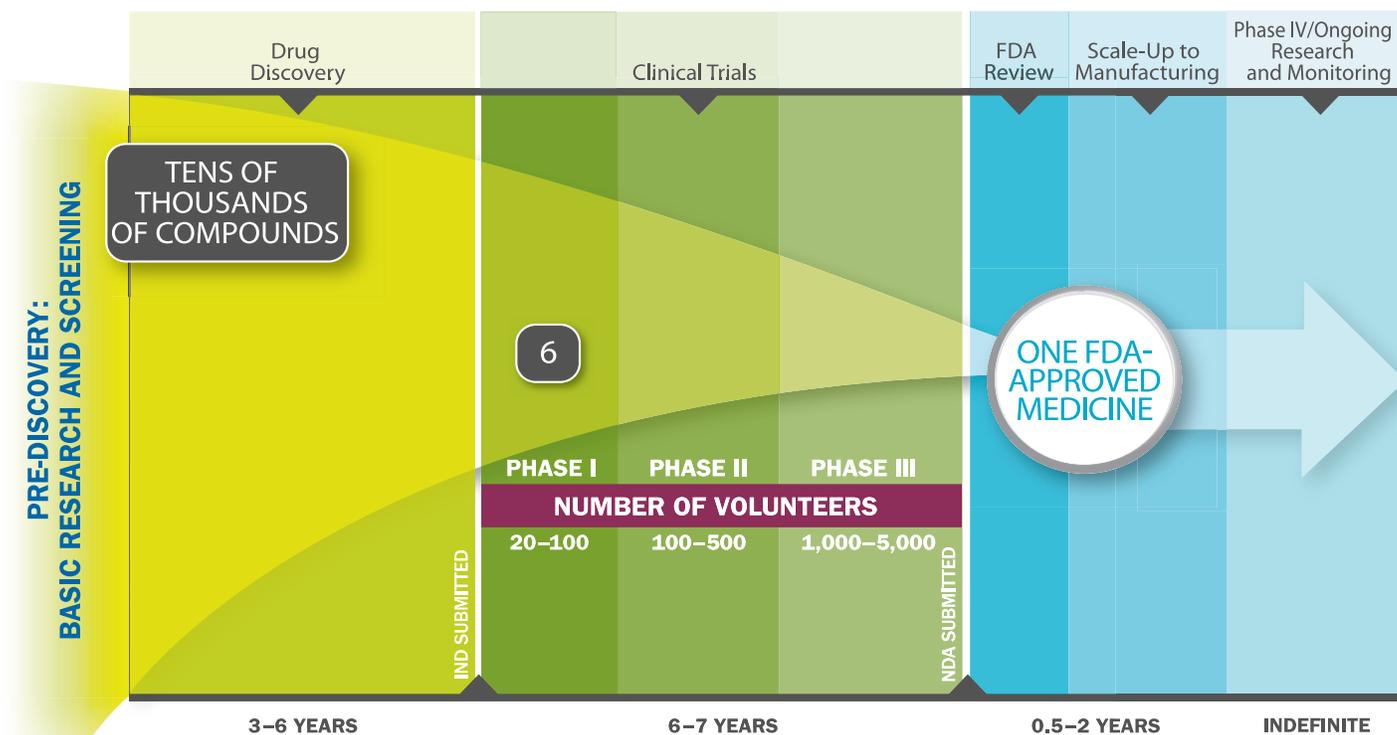
Provided as a public service by PhRMA. Founded in 1958 as the Pharmaceutical Manufacturers Association.

Copyright © 2014 by the Pharmaceutical Research and Manufacturers of America. Permission to reprint is awarded if proper credit is given.

**Pharmaceutical Research and Manufacturers of America** • 950 F Street, NW, Suite 300, Washington, DC 20004

# The Drug Discovery, Development and Approval Process

Developing a new medicine takes an average of 10-15 years.  
Of the tens of thousands of compounds screened, only one is 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. Tens of thousands of compounds may be screened early in development, but only one ultimately receives approval. Even medicines that reach clinical trials have only a 16 percent chance of being approved.

On average, it costs a company \$1.2 billion, including the cost of failures, 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. More recent studies estimate the cost to be even higher.

Once a new compound has been identified in the laboratory, medicines are usually 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 com-

pany 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**—Researchers test the drug in a small group of people, usually between 20 and 100 healthy adult volunteers, to evaluate its initial safety and tolerability profile, determine a safe dosage range, and identify potential side effects.

**Clinical Trials, Phase II**—The drug is given to volunteer patients, usually between 100 and 500, to see if it is effective, identify an optimal dose, and to further evaluate its short-term safety.

**Clinical Trials, Phase III**—The drug is given to a larger, more diverse patient population, often involving between 1,000 and 5,000 patients

(but sometime many more thousands), to generate statistically significant evidence to confirm its safety and effectiveness. They are the longest studies, and usually take place in multiple sites around the world.

**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.

**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 \$51.1 billion in research and development in 2013.