

Arthritis

PRESENTED BY AMERICA'S BIOPHARMACEUTICAL RESEARCH COMPANIES

Biopharmaceutical Research Companies are Developing Nearly 200 Medicines for the Most Common Chronic Health Problem in the United States

America's biopharmaceutical research companies are currently developing 198 medicines to help the more than 50 million Americans afflicted with at least one of the 100 different musculoskeletal disorders, including arthritis. All of the medicines are either in clinical trials or awaiting review by the U.S. Food and Drug Administration.

Arthritis is the most common cause of disability in the United States. Each year, it is responsible for 44 million outpatient doctor visits, nearly 1 million hospitalizations, and nearly 10,000 deaths. And it costs the American economy nearly \$128 billion annually in direct medical costs and indirect costs, such as lost wages and productivity.

By 2030, it is estimated that the number of Americans with some form of diagnosed arthritis will increase to more than 67 million. "As the baby boomer generation ages, advances in research and the development of more effective and safer treatments are critical to helping improve the quality of life for millions of people with arthritis," said John Howard Klippel, M.D., president and CEO of the Arthritis Foundation.

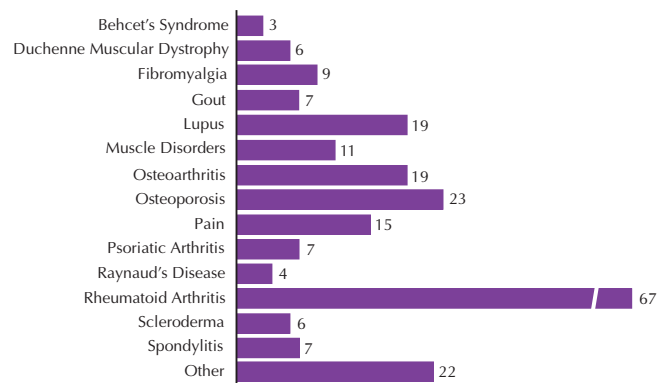
New medicines today in the research and development pipeline offer hope of reducing the human and economic costs of the many musculoskeletal disorders affecting Americans. They include:

- 67 for rheumatoid arthritis that affects about 1.3 million American adults.
- 23 for osteoporosis that affects 10 million people, 80 percent of whom are women.
- 19 for lupus which affects an estimated 1.5 million Americans.
- 19 for osteoarthritis, the most common form of arthritis, affecting nearly 27 million Americans.
- 15 for musculoskeletal pain that affects the muscles, ligaments, tendons, and bones.
- 9 for fibromyalgia which affects 3 million to 6 million Americans.

Examples of some medicines now being tested to treat musculoskeletal disorders include:

- A new monoclonal antibody in development for lupus modulates B-cells that produce antibodies against the

MEDICINES AND VACCINES IN DEVELOPMENT FOR ARTHRITIS*



* Some medicines are listed in more than one category.

body's own cells and tissue, causing the immune system to turn on itself.

- A medicine in development for rheumatoid arthritis (RA) that inhibits two types of an enzyme that are key components in signaling activation of cytokines and growth factors that are elevated in patients with RA.
- A potential first-in-class medicine in development for pain associated with osteoarthritis that is an inhibitor of a gene-encoding protein that plays a role in inflammatory pain.

Researching and developing new medicines remains a risky investment and lengthy process—costing, on average, \$1.2 billion, including the cost of failures, and taking between 10–15 years to bring a new medicine to patients. But advances in our understanding of diseases and how to treat them have allowed America's biopharmaceutical research companies to conduct the cutting-edge research needed to reduce the destructive toll of arthritis and other musculoskeletal disorders and to allow more patients to lead healthier, happier, more productive lives.

John J. Castellani
President and CEO
PhRMA

Medicines in Development for Arthritis

BEHCET'S SYNDROME

Product Name	Company	Indication	Development Status*
apremilast	Celgene <i>Summit, NJ</i>	Behcet's syndrome (see also psoriatic arthritis, rheumatoid arthritis, spondylitis)	Phase II (908) 673-9000
gevokizumab (XOMA052)	XOMA <i>Berkeley, CA</i>	Behcet's syndrome (see also rheumatoid arthritis)	Phase II (510) 204-7200
Veldona [®] interferon-alpha lozenge (Orphan Drug)	Amarillo Biosciences <i>Amarillo, TX</i>	Behcet's syndrome (see also fibromyalgia)	Phase II (806) 376-1741

DUCHENNE MUSCULAR DYSTROPHY

Product Name	Company	Indication	Development Status
ACE-031 (Orphan Drug)	Acceleron Pharma <i>Cambridge, MA</i>	Duchenne muscular dystrophy	Phase II (617) 649-9200
ataluren (PTC124) (Orphan Drug)	Genzyme <i>Cambridge, MA</i> PTC Therapeutics <i>South Plainfield, NJ</i>	Duchenne muscular dystrophy (Fast Track)	Phase II/III (617) 252-7500 (908) 222-7000
eteplirsen (AVI-4658) (Orphan Drug)	AVI BioPharma <i>Bothell, WA</i>	Duchenne muscular dystrophy	Phase II (425) 354-5038
GSK2402968 (antisense oligonucleotide) (Orphan Drug)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i> Prosensa <i>Leiden, The Netherlands</i>	Duchenne muscular dystrophy	Phase III (888) 825-5249
idebenone (Orphan Drug)	Santhera Pharmaceuticals <i>Charlestown, MA</i>	Duchenne muscular dystrophy (see also other)	Phase III (617) 886-5161
muscular dystrophy gene therapy	Asklepios BioPharmaceutical <i>Chapel Hill, NC</i>	Duchenne muscular dystrophy	Phase I (919) 968-2727

FIBROMYALGIA

Product Name	Company	Indication	Development Status
AGN-XX/YY (rezatomidine)	ACADIA Pharmaceuticals <i>San Diego, CA</i> Allergan <i>Irvine, CA</i>	fibromyalgia	Phase II (858) 558-2871 (800) 433-8871
Cymbalta [®] duloxetine	Eli Lilly <i>Indianapolis, IN</i>	juvenile primary fibromyalgia syndrome	Phase III (800) 545-5979
droxidopa	Chelsea Therapeutics <i>Charlotte, NC</i>	fibromyalgia	Phase II (704) 341-1516

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

FIBROMYALGIA

Product Name	Company	Indication	Development Status
flupirtine	Adeona Pharmaceuticals <i>Ann Arbor, MI</i> Meda Pharmaceuticals <i>Somerset, NJ</i>	fibromyalgia	Phase II (734) 332-7800 (732) 564-2200
Lyrica® CR pregabalin (controlled-release)	Pfizer <i>New York, NY</i>	fibromyalgia	Phase II/III (860) 723-5156
Neupro® rotigotine transdermal	UCB <i>Smyrna, GA</i>	fibromyalgia	Phase II (770) 970-7500
TNX-102 (cyclobenzaprine very low dose)	TONIX Pharmaceuticals <i>New York, NY</i>	fibromyalgia syndrome	Phase II (212) 980-9155
Veldona® interferon-alpha lozenge	Amarillo Biosciences <i>Amarillo, TX</i>	fibromyalgia (see also Behcet's syndrome)	Phase II (806) 376-1741
Vimpat® lacosamide	UCB <i>Smyrna, GA</i>	fibromyalgia	Phase II completed (770) 970-7500

GOUT

Product Name	Company	Indication	Development Status
Arcalyst® rilonacept	Regeneron Pharmaceuticals <i>Tarrytown, NY</i>	gout	Phase III (877) 734-6777
BCX-4208	BioCryst Pharmaceuticals <i>Birmingham, AL</i>	gout	Phase II (205) 444-4600
Ilaris® canakinumab (subcutaneous)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	gouty arthritis (see also osteoarthritis, rheumatoid arthritis)	application submitted (888) 669-6682
lesinurad	Ardea Biosciences <i>San Diego, CA</i>	gout	Phase II (858) 652-6500
MBX-102 (arhalofenate)	Metabolex <i>Hayward, CA</i>	gout	Phase II (510) 293-8800
NU1618 (tranilast/allopurinol)	Nuon Therapeutics <i>San Mateo, CA</i>	gout	Phase II (650) 645-1800
pegadricase	3SBio <i>Shenyang, China</i>	gout	Phase I www.3sbio.com

LUPUS

Product Name	Company	Indication	Development Status
A-623	Anthera Pharmaceuticals <i>Hayward, CA</i>	systemic lupus erythematosus	Phase II (510) 856-5600
AGS-009	Argos Therapeutics <i>Durham, NC</i>	systemic lupus erythematosus	Phase I (919) 287-6300
AMG 557	Amgen <i>Thousand Oaks, CA</i>	systemic lupus erythematosus	Phase I (800) 772-6436

LUPUS

Product Name	Company	Indication	Development Status
AMG 811	Amgen <i>Thousand Oaks, CA</i>	systemic lupus erythematosus	Phase I (800) 772-6436
atacipept (anti-Blys/anti-APRIL fusion protein)	EMD Serono <i>Rockland, MA</i>	systemic lupus erythematosus	Phase III (800) 283-8088
BAFF antibody (LY2127399)	Eli Lilly <i>Indianapolis, IN</i>	systemic lupus erythematosus (see also rheumatoid arthritis)	Phase III (800) 545-5979
Benlysta [®] belimumab (subcutaneous)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i> Human Genome Sciences <i>Rockville, MD</i>	systemic lupus erythematosus (see also other)	Phase II (888) 825-5249 (301) 309-8504
CDP-7657 (CD40L)	Biogen Idec <i>Cambridge, MA</i>	systemic lupus erythematosus	Phase I (617) 679-2000
CNTO-136 (sirukumab)	Centocor Ortho Biotech <i>Horsham, PA</i>	lupus (see also rheumatoid arthritis)	Phase II (610) 651-6000
DV-1179	Dynavax Technologies <i>Berkeley, CA</i>	systemic lupus erythematosus	Phase I (877) 848-5100
epratuzumab	Immunomedics <i>Morris Plains, NJ</i> UCB <i>Smyrna, GA</i>	systemic lupus erythematosus (Fast Track)	Phase III (973) 605-8200
forigerimod (CEP-33457)	Cephalon <i>Frazer, PA</i>	systemic lupus erythematosus	Phase III (610) 344-0200
laquinimod	Teva Neuroscience <i>North Wales, PA</i>	systemic lupus erythematosus	Phase II (800) 838-2872
MEDI-545 (anti-IFN-alpha mAb)	AstraZeneca <i>Wilmington, DE</i> Medarex <i>Princeton, NJ</i> MedImmune <i>Gaithersburg, MD</i>	systemic lupus erythematosus	Phase II (800) 236-9933 (609) 430-2880 (301) 298-0000
MEDI-570 (anti-ICOS mAb)	AstraZeneca <i>Wilmington, DE</i> MedImmune <i>Gaithersburg, MD</i>	systemic lupus erythematosus	Phase I (301) 298-0000
Orencia [®] abatacept (intravenous)	Bristol-Myers Squibb <i>Princeton, NJ</i>	systemic lupus erythematosus (see also rheumatoid arthritis)	Phase II/III (212) 546-4000
PF-04236921	Pfizer <i>New York, NY</i>	lupus (see also rheumatoid arthritis)	Phase I (860) 732-5156
RG7415 (rontalizumab)	Genentech <i>South San Francisco, CA</i>	systemic lupus erythematosus	Phase II (800) 626-3553
SBI-087 (PF-05230895)	Emergent BioSolutions <i>Rockville, MD</i> Pfizer <i>New York, NY</i>	systemic lupus erythematosus (see also rheumatoid arthritis)	Phase I (301) 795-1800 (860) 732-5156

MUSCLE DISORDERS

Product Name	Company	Indication	Development Status
AMG 745	Amgen <i>Thousand Oaks, CA</i>	muscular atrophy	Phase I (800) 772-6436
arbaclofen placarbil (XP19986)	XenoPort <i>Santa Clara, CA</i>	muscle spasticity	Phase II www.xenoport.com
Botox® onabotulinum toxin A (Orphan Drug)	Allergan <i>Irvine, CA</i>	muscle spasticity ----- muscle spasm	application submitted (714) 246-4500 Phase III (714) 246-4500
CK-2017357	Cytokinetics <i>South San Francisco, CA</i>	muscle fatigue	Phase II (650) 624-3000
Dysport® abobotulinum toxin A for injection	Tercica <i>Brisbane, CA</i>	focal spasticity of upper and lower limb in adults and children	Phase III (650) 624-4900
GSK2245840 (SIRT1 protein stimulant)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	muscular atrophy	Phase I (888) 825-5249
GTx-024	GTx <i>Memphis, TN</i>	muscular atrophy	Phase II completed (901) 523-9700
IPX-056 (baclofen extended-release)	Impax Laboratories <i>Hayward, CA</i>	muscle spasticity in patients with multiple sclerosis	Phase III (510) 240-6000
LY2495655 (anti-myostatin mAb)	Eli Lilly <i>Indianapolis, IN</i>	muscular atrophy	Phase II (800) 545-5979
nabilone	Valeant Pharmaceuticals International <i>Irvine, CA</i>	muscle spasticity	Phase II (800) 548-5100
nabiximols	Otsuka America Pharmaceutical <i>Rockville, MD</i>	muscle spasticity	Phase II (800) 562-3974

OSTEOARTHRITIS

Product Name	Company	Indication	Development Status
Ampion™	Ampio Pharmaceuticals <i>Greenwood Village, CO</i>	osteoarthritis	Phase I (303) 418-1000
BI 113823	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	osteoarthritis	Phase I (800) 243-0127
CG-100649	CG Pharmaceuticals <i>Emeryville, CA</i>	inflammation associated with osteoarthritis	Phase I (510) 594-8200
fibroblast growth factor-18	EMD Serono <i>Rockland, MA</i>	osteoarthritis (see also other)	Phase I (800) 283-8088

OSTEOARTHRITIS

Product Name	Company	Indication	Development Status
IBU-PC	PLx Pharma <i>Houston, TX</i>	pain and inflammation associated with osteoarthritis	Phase II (713) 842-1249
Ilaris [®] canakinumab (intra-arterial)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	osteoarthritis (see also gout, rheumatoid arthritis)	Phase II (888) 669-6682
IP-880	Iroko Pharmaceuticals <i>Philadelphia, PA</i>	osteoarthritis	Phase I (267) 546-3003
IP-889	Iroko Pharmaceuticals <i>Philadelphia, PA</i>	osteoarthritis	Phase III (267) 546-3003
LT-NS001 (naproxen etemesil)	Logical Therapeutics <i>Waltham, MA</i>	osteoarthritis	Phase II/III (781) 290-0900
MEDI-578 (anti-NGF mAb)	AstraZeneca <i>Wilmington, DE</i> MedImmune <i>Gaithersburg, MD</i>	osteoarthritic pain	Phase I (800) 236-9933 (301) 298-0000
naproxcinod	NicOx <i>Sophia Antipolis, France</i>	osteoarthritis	application submitted www.nicox.com
osteoarthritis compound (LY2828360)	Eli Lilly <i>Indianapolis, IN</i>	osteoarthritis	Phase II (800) 545-5979
SAR113945 (IKK-β inhibitor)	sanofi-aventis <i>Bridgewater, NJ</i>	osteoarthritis	Phase I (800) 633-1610
SAR114137 (cathespain S/K inhibitor)	sanofi-aventis <i>Bridgewater, NJ</i>	osteoarthritic pain	Phase I (800) 633-1810
SAR292833 (GRC15300) TRPV3 antagonist	sanofi-aventis <i>Bridgewater, NJ</i> Glenmark Pharmaceuticals <i>Mumbai, India</i>	osteoarthritic pain	Phase I (800) 633-1810
SD-6010	Pfizer <i>New York, NY</i>	osteoarthritis	Phase II/III (860) 732-5156
SMC021 (calcitonin oral)	Emisphere Technologies <i>Tarrytown, NY</i> Novartis Pharmaceuticals <i>East Hanover, NJ</i>	osteoarthritis (see also osteoporosis)	Phase III (914) 347-2220 (888) 669-6682
Synavive [™] prednisone/ dipyridamole	Zaliscus <i>Cambridge, MA</i>	osteoarthritis (see also rheumatoid arthritis)	Phase II completed (617) 301-7000
TG-C	TissueGene <i>Rockville, MD</i>	osteoarthritis	Phase I (301) 921-6000

OSTEOPOROSIS

Product Name	Company	Indication	Development Status
ACE-011 (sotatercept)	Acceleron Pharma <i>Cambridge, MA</i> Celgene <i>Summit, NJ</i>	postmenopausal osteoporosis	Phase I (617) 649-9200 (908) 673-9000

OSTEOPOROSIS

Product Name	Company	Indication	Development Status
alendronate effervescent (EX101)	Nycomed US <i>Melville, NY</i> EffRx <i>Lausanne, Switzerland</i>	osteoporosis	application submitted (631) 454-7677 www.effrx.com
AMG 785 (anti-sclerostin mAb)	Amgen <i>Thousand Oaks, CA</i>	postmenopausal osteoporosis (see also other)	Phase II (800) 772-6436
Aprala TM bazedoxifene/ conjugated estrogens	Ligand Pharmaceuticals <i>San Diego, CA</i> Pfizer <i>New York, NY</i>	postmenopausal osteoporosis prevention	Phase III (858) 550-7500 (860) 732-5156
AUS-131	Ausio Pharmaceuticals <i>Cincinnati, OH</i>	osteoporosis	Phase I (513) 731-1600
BA-058	Radius Health <i>Cambridge, MA</i>	osteoporosis (subcutaneous)	Phase II (617) 551-4700
		osteoporosis (transdermal)	Phase I (617) 551-4700
calcitonin oral	Tarsa Therapeutics <i>Philadelphia, PA</i>	postmenopausal osteoporosis treatment	Phase III completed (267) 273-7940
		postmenopausal osteoporosis prevention	Phase II (267) 273-7940
DP-001	Deltanoid Pharmaceuticals <i>Madison, WI</i>	osteoporosis	Phase II (608) 238-7710
GSK768974 (parathyroid hormone receptor agonist)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i> Unigene <i>Boonton, NJ</i>	postmenopausal osteoporosis	Phase II (888) 825-5249 (973) 265-1100
MER-103 (oral alendronic acid)	Merrion Pharmaceuticals <i>Wilmington, DE</i>	osteoporosis	Phase II completed (910) 799-1847
MK-5442 (CaSR antagonist)	Merck <i>Whitehouse Station, NJ</i>	osteoporosis	Phase II (800) 672-6372
odanacatib (MK-0822)	Merck <i>Whitehouse Station, NJ</i>	male osteoporosis, postmenopausal osteoporosis	Phase III (800) 672-6372
osteoporosis compound (LY2541546)	Eli Lilly <i>Indianapolis, IN</i>	osteoporosis	Phase II (800) 545-5979
PF-04840082 (DKK1 protein inhibitor)	Pfizer <i>New York, NY</i>	osteoporosis treatment and prevention	Phase I (860) 732-5156
Prolia [®] denosumab	Amgen <i>Thousand Oaks, CA</i>	male osteoporosis (see also rheumatoid arthritis)	Phase III (800) 772-6436
Reclast [®] zoledronic acid	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	corticosteroid-induced osteoporosis, postmenopausal osteoporosis prevention	application submitted (888) 669-6682

OSTEOPOROSIS

Product Name	Company	Indication	Development Status
SMC021 (calcitonin oral)	Emisphere Technologies Tarrytown, NY Novartis Pharmaceuticals East Hanover, NJ	postmenopausal osteoporosis (see also osteoarthritis)	Phase III (914) 347-2220 (888) 669-6682
teriparatide intranasal	Marina Biotech Bothell, WA	osteoporosis	Phase II (425) 908-3600
teriparatide oral (PTH134)	Emisphere Technologies Tarrytown, NY Novartis Pharmaceuticals East Hanover, NJ	postmenopausal osteoporosis	Phase I (914) 347-2220 (888) 669-6682
teriparatide transdermal (ZP-PTH)	Zosana Pharma Fremont, CA	osteoporosis	Phase II (510) 745-1200
ViaDor-hPTH (1-34) (teriparatide transdermal)	Eli Lilly Indianapolis, IN TransPharma Medical Lod, Israel	osteoporosis	Phase I (800) 545-5979
Viviant™ bazedoxifene	Ligand Pharmaceuticals San Diego, CA Pfizer New York, NY	postmenopausal osteoporosis prevention and treatment	application submitted (858) 550-7500 (860) 732-5156
ZT-034 (teriparatide)	Zelos Therapeutics West Conshohocken, PA	osteoporosis (intranasal)	Phase I (610) 260-6045
		osteoporosis (subcutaneous)	Phase I (610) 260-6045

PAIN

Product Name	Company	Indication	Development Status
ABT-652	Abbott Laboratories Abbott Park, IL	musculoskeletal pain	Phase II (847) 937-6100
BEMA® Buprenorphine buprenorphine transmucosal	BioDelivery Sciences International Raleigh, NC	back pain, musculoskeletal pain	Phase III (919) 582-9050
bupivacaine transdermal	DURECT Cupertino, CA	back pain	Phase II completed (408) 777-1417
chondrocyte tissue grafts	ISTO Technologies St. Louis, MO	back pain	Phase I (314) 995-6049
diclofenac transdermal second-generation	Nuvo Research Mississauga, Canada	musculoskeletal pain	Phase II (905) 673-6980
EXPAREL™ bupivacaine extended-release liposome injection	Pacira Pharmaceuticals Parsippany, NJ	musculoskeletal pain	Phase I (973) 254-3560

PAIN

Product Name	Company	Indication	Development Status
fulranumab	Johnson & Johnson Pharmaceutical Research & Development <i>Raritan, NJ</i>	back pain	Phase II (800) 817-5286
FX005	Flexion Therapeutics <i>Woburn, MA</i>	musculoskeletal pain	Phase I/II (781) 897-9977
IDEA-033 (ketoprofen transdermal)	IDEA <i>Munich, Germany</i>	musculoskeletal pain	Phase III www.idea-ag.de
JNJ-39439335 (TRPV1 receptor antagonist)	Johnson & Johnson Pharmaceutical Research & Development <i>Raritan, NJ</i>	musculoskeletal pain	Phase I (800) 817-5286
ketoprofen transdermal	Hisamitsu Pharmaceutical <i>Tokyo, Japan</i>	musculoskeletal pain	Phase III www.hisamitsu.co.jp
Opana® ER oxymorphone	Endo Pharmaceuticals <i>Chadd's Farm, PA</i>	musculoskeletal pain (abuse-resistant)	application submitted (610) 558-9800
oxycodone/ naloxone controlled release	Mundipharma <i>Basel, Switzerland</i> Purdue Pharma <i>Stamford, CT</i>	back pain	Phase II (203) 588-8000
tapentadol controlled-release	Johnson & Johnson Pharmaceutical Research & Development <i>Raritan, NJ</i>	musculoskeletal pain	application submitted (800) 817-5286
ZX002 (hydrocodone controlled-release)	Zogenix <i>San Diego, CA</i>	back pain	Phase III (866) 964-3649

PSORIATIC ARTHRITIS

Product Name	Company	Indication	Development Status
apremilast	Celgene <i>Summit, NJ</i>	psoriatic arthritis (see also Behcet's syndrome, rheumatoid arthritis, spondylitis)	Phase III (908) 673-9000
Cimzia® certolizumab pegol	UCB <i>Smyrna, GA</i>	psoriatic arthritis (see also spondylitis)	Phase III (770) 970-7500
RG4934 (anti-IL-17 mAb)	Roche <i>Nutley, NJ</i>	psoriatic arthritis	Phase I (973) 235-5000
RO5310074	Roche <i>Nutley, NJ</i>	psoriatic arthritis	Phase I (973) 235-5000
secukinumab	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	psoriatic arthritis (see also rheumatoid arthritis, spondylitis)	Phase II (888) 669-6682
Stelara® ustekinumab	Centocor Ortho Biotech <i>Horsham, PA</i>	psoriatic arthritis	Phase III (610) 651-6000
tofacitinib (CP-690550)	Pfizer <i>New York, NY</i>	psoriatic arthritis (see also rheumatoid arthritis, spondylitis)	Phase II (860) 732-5156

RAYNAUD'S DISEASE

Product Name	Company	Indication	Development Status
MQX-503 (nitroglycerin topical)	MediQuest Therapeutics <i>Bothell, WA</i>	Raynaud's disease	Phase III (425) 398-9580
PF-00489791	Pfizer <i>New York, NY</i>	Raynaud's disease	Phase II (860) 732-5156
Revatio [®] sildenafil	Pfizer <i>New York, NY</i>	Raynaud's disease	in clinical trials (860) 732-5156
SLX-2101	Kadmon Pharmaceuticals <i>New York, NY</i> Nano Terra <i>Brighton, MA</i>	Raynaud's disease	Phase II (212) 600-1902 (617) 621-8500

RHEUMATOID ARTHRITIS

Product Name	Company	Indication	Development Status
Actemra [™] tocilizumab	Genentech <i>South San Francisco, CA</i>	early-stage rheumatoid arthritis (intravenous) (see also spondylitis)	Phase III (800) 626-3553
		rheumatoid arthritis (subcutaneous)	Phase III (800) 626-3553
anti-LT alpha (RG7416)	Genentech <i>South San Francisco, CA</i>	rheumatoid arthritis	Phase II (800) 626-3553
anti-TWEAK (BIIB 023)	Biogen Idec <i>Cambridge, MA</i>	rheumatoid arthritis	Phase I completed (617) 679-2000
apremilast	Celgene <i>Summit, NJ</i>	rheumatoid arthritis (see also Behcet's syndrome, psoriatic arthritis, spondylitis)	Phase II (908) 673-9000
Arcoxia [™] etoricoxib	Merck <i>Whitehouse Station, NJ</i>	rheumatoid arthritis (see also spondylitis)	Phase III (800) 672-6372
ARG301	arGentis Pharmaceuticals <i>Memphis, TN</i>	rheumatoid arthritis	Phase I (901) 818-3262
ASP2408 (CTLA4-Ig fusion protein)	Astellas Pharma US <i>Deerfield, IL</i> Perseid Therapeutics <i>Redwood City, CA</i>	rheumatoid arthritis	Phase I (800) 695-4321 (650) 298-5800
AVL-292	Avila Therapeutics <i>Waltham, MA</i>	rheumatoid arthritis	Phase I (781) 891-0086
BAFF antibody (LY2127399)	Eli Lilly <i>Indianapolis, IN</i>	rheumatoid arthritis (subcutaneous) (see also lupus)	Phase III (800) 545-5979
		rheumatoid arthritis (intravenous)	Phase II (800) 545-5979
BG-12 (dimethyl fumarate)	Biogen Idec <i>Cambridge, MA</i>	rheumatoid arthritis	Phase II (617) 679-2000

RHEUMATOID ARTHRITIS

Product Name	Company	Indication	Development Status
BMS-817399 (CCR1 antagonist)	Bristol-Myers Squibb <i>Princeton, NJ</i>	rheumatoid arthritis	Phase I (212) 546-4000
BMS-945429 (anti-IL6)	Bristol-Myers Squibb <i>Princeton, NJ</i> Alder Biopharmaceuticals <i>Bothell, WA</i>	rheumatoid arthritis	Phase II (212) 546-4000 (425) 205-2900
CAM-3001 (mavrilimumab)	AstraZeneca <i>Wilmington, DE</i> MedImmune <i>Gaithersburg, MD</i>	rheumatoid arthritis	Phase II (800) 236-9933 (301) 398-0000
CCX354	ChemoCentryx <i>Mountain View, CA</i>	rheumatoid arthritis	Phase II (650) 210-2900
cenplacel-L (PDA-001)	Celgene Cellular Therapeutics <i>Summit, NJ</i>	rheumatoid arthritis	Phase I/II (908) 673-9000
CF101	Can-Fite BioPharma <i>Petah-Tikva, Israel</i>	rheumatoid arthritis	Phase II www.canfite.com
CH-4051	Chelsea Therapeutics <i>Charlotte, NC</i>	rheumatoid arthritis	Phase II (704) 341-1516
CNTO-136 (sirukumab)	Centocor Ortho Biotech <i>Horsham, PA</i>	rheumatoid arthritis (see also lupus)	Phase II (610) 651-6000
EVT 401	Evotec <i>North Potomac, MD</i>	rheumatoid arthritis	Phase I completed (240) 683-1199
fezakinumab (ILV-094)	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase II (860) 732-5156
fostamatinib	AstraZeneca <i>Wilmington, DE</i> Rigel Pharmaceuticals <i>South San Francisco, CA</i>	rheumatoid arthritis	Phase III (800) 236-9933 (650) 624-1100
gevokizumab (XOMA052)	XOMA <i>Berkeley, CA</i>	rheumatoid arthritis (see also Behcet's syndrome)	Phase II (510) 204-7200
GSK315234 (oncostatin M mAb)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	rheumatoid arthritis	Phase II (888) 825-5249
HE3286	Hollis-Eden Pharmaceuticals <i>San Diego, CA</i>	rheumatoid arthritis	Phase I/II completed (858) 587-9333
Humira® adalimumab	Abbott Laboratories <i>Abbott Park, IL</i>	rheumatoid arthritis (combination therapy)	Phase III (847) 937-6100
IL-17 antibody (ixekizumab)	Eli Lilly <i>Indianapolis, IN</i>	rheumatoid arthritis	Phase II (800) 545-5979
Ilaris® canakinumab (subcutaneous) (Orphan Drug)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	systemic juvenile idiopathic arthritis (see also gout, osteoarthritis)	Phase III (888) 669-6682
JAK-1/JAK-2 (LY3009104)	Eli Lilly <i>Indianapolis, IN</i>	rheumatoid arthritis	Phase II (800) 545-5979
JNJ-40346527	Johnson & Johnson Pharmaceutical Research & Development <i>Raritan, NJ</i>	rheumatoid arthritis	Phase I (800) 817-5286

RHEUMATOID ARTHRITIS

Product Name	Company	Indication	Development Status
KB002/003 (anti-GM-CSF)	KaloBios Pharmaceuticals <i>South San Francisco, CA</i>	rheumatoid arthritis	Phase II (650) 243-3100
Lodotra® prednisone controlled-release	Horizon Pharma <i>Northbrook, IL</i>	rheumatoid arthritis	Phase III completed (224) 383-3000
LX2931	Lexicon Pharmaceuticals <i>The Woodlands, TX</i>	rheumatoid arthritis	Phase II (281) 863-3000
methotrexate subcutaneous auto-injection	Antares Pharma <i>Ewing, NJ</i>	rheumatoid arthritis	Phase I (609) 359-3020
NN8209 (anti-C5aR mAb)	Novo Nordisk <i>Princeton, NJ</i>	rheumatoid arthritis	Phase II (609) 987-5800
NN8226 (anti-IL-20 antibody)	Novo Nordisk <i>Princeton, NJ</i>	rheumatoid arthritis	Phase II (609) 987-5800
NN8555 (mAb)	Novo Nordisk <i>Princeton, NJ</i>	rheumatoid arthritis	Phase II (609) 987-5800
NN8828 (anti-IL-21 mAb)	Novo Nordisk <i>Princeton, NJ</i>	rheumatoid arthritis	Phase I (609) 987-5800
NU3450 (tranilast)	Nuon Therapeutics <i>San Mateo, CA</i>	rheumatoid arthritis	Phase II (650) 645-1800
ofatumumab (HuMax-CD20)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i>	rheumatoid arthritis (intravenous)	Phase II (888) 825-5249
		rheumatoid arthritis (subcutaneous)	Phase II (888) 825-5249
olokizumab	UCB <i>Smyrna, GA</i>	rheumatoid arthritis (subcutaneous)	Phase II (770) 970-7500
		rheumatoid arthritis (intravenous)	Phase I/II completed (770) 970-7500
Oralgam™ oral human gammaglobulin (Orphan Drug)	Latona Life Sciences <i>Phoenix, AZ</i>	juvenile rheumatoid arthritis, rheumatoid arthritis	Phase II completed (480) 254-8530
Orencia® abatacept (subcutaneous)	Bristol-Myers Squibb <i>Princeton, NJ</i>	moderate to severe rheumatoid arthritis (see also lupus)	application submitted (212) 546-4000
otelixizumab (GSK2136525)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i> Tolerx <i>Cambridge, MA</i>	rheumatoid arthritis	Phase II (888) 825-5249 (617) 354-8100
ozoralizumab (ATN-103)	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase II (860) 732-5156
PF-04171327	Pfizer <i>New York, NY</i>	rheumatoid arthritis	Phase II (860) 732-5156
PF-04236921	Pfizer <i>New York, NY</i>	rheumatoid arthritis (see also lupus)	Phase I (860) 732-5156

RHEUMATOID ARTHRITIS

Product Name	Company	Indication	Development Status
PF-05230905 (ATN-192)	Pfizer New York, NY	rheumatoid arthritis	Phase I (860) 732-5156
PLX3397	Plexxikon Berkeley, CA	rheumatoid arthritis	Phase I (510) 647-4000
PLX5622	Plexxikon Berkeley, CA	rheumatoid arthritis	Phase I (510) 647-4000
PMI-001	Phytomedics Jamesburg, NJ	rheumatoid arthritis	Phase II completed (609) 655-0715
PRO-515	Cypress Bioscience San Diego, CA	rheumatoid arthritis	Phase II (858) 452-2323
Prolia [®] denosumab	Amgen Thousand Oaks, CA	rheumatoid arthritis (see also osteoporosis)	Phase II (800) 772-6436
PRTX-100 (staphylococcal protein A)	Protalex New Hope, PA	rheumatoid arthritis	Phase I (215) 862-9720
RPI-78	ReceptoPharm Plantation, FL	rheumatoid arthritis	Phase I (954) 321-8988
RX-10001	Resolvix Pharmaceuticals Cambridge, MA	rheumatoid arthritis	Phase I (781) 541-5045
SAN-300 (anti-VLA-1 antibody)	Santarus San Diego, CA	rheumatoid arthritis	Phase I (858) 314-5700
SAR153191 (anti-IL-6R mAb)	Regeneron Pharmaceuticals Tarrytown, NY sanofi-aventis Bridgewater, NJ	rheumatoid arthritis (see also spondylitis)	Phase III (914) 345-7400 (800) 633-1610
SBI-087 (PF-05230895)	Emergent BioSolutions Rockville, MD Pfizer New York, NY	rheumatoid arthritis (see also lupus)	Phase II (301) 795-1800 (860) 732-5156
SCH-900117 (IL-17 inhibitor)	Merck Whitehouse Station, NJ	rheumatoid arthritis	Phase I (800) 672-6372
secukinumab	Novartis Pharmaceuticals East Hanover, NJ	rheumatoid arthritis (subcutaneous) (see also psoriatic arthritis, spondylitis)	Phase II (888) 669-6682
		rheumatoid arthritis (intravenous)	Phase I/II (888) 669-6682
Simponi [™] golimumab	Centocor Ortho Biotech Horsham, PA	rheumatoid arthritis (intravenous)	Phase III (610) 651-6000
		juvenile rheumatoid arthritis (subcutaneous)	Phase III (610) 651-6000
Synavive [™] prednisone/ dipyridamole	Zaliscus Cambridge, MA	rheumatoid arthritis (see also osteoarthritis)	Phase II completed (617) 301-7000

RHEUMATOID ARTHRITIS

Product Name	Company	Indication	Development Status
T-5224	Toyama Chemical <i>Tokyo, Japan</i>	rheumatoid arthritis	Phase I
tofacitinib (CP-690550)	Pfizer <i>New York, NY</i>	rheumatoid arthritis (see also psoriatic arthritis, spondylitis)	Phase III (860) 732-5156
veltuzumab	Immunomedics <i>Morris Plains, NJ</i> Nycomed <i>Zurich, Switzerland</i>	rheumatoid arthritis	Phase II (973) 605-8200 www.nycomed.com
VGX-1027	Inovio Pharmaceuticals <i>Blue Bell, PA</i>	rheumatoid arthritis	Phase I completed (267) 440-4200
VX-509	Vertex Pharmaceuticals <i>Cambridge, MA</i>	rheumatoid arthritis	Phase II (877) 634-8789

SCLERODERMA

Product Name	Company	Indication	Development Status
ARG201 (Orphan Drug)	arGentis Pharmaceuticals <i>Memphis, TN</i>	systemic scleroderma	Phase II (901) 552-4730
CC-10015	Celgene <i>Summit, NJ</i>	systemic scleroderma	Phase I (908) 673-9000
Gleevec® imatinib	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	scleroderma	Phase II (888) 669-6682
MEDI-546 (anti-IFNalphaR mAb)	AstraZeneca <i>Wilmington, DE</i> Medarex <i>Princeton, NJ</i> MedImmune <i>Gaithersburg, MD</i>	scleroderma	Phase I (800) 236-9933 (301) 298-0000
MEDI-551 (anti-CD19 mAb)	AstraZeneca <i>Wilmington, DE</i> MedImmune <i>Gaithersburg, MD</i>	scleroderma	Phase I (800) 236-9933 (301) 298-0000
treprostinil	United Therapeutics <i>Silver Spring, MD</i>	systemic scleroderma	Phase II (301) 608-9292

SPONDYLITIS

Product Name	Company	Indication	Development Status
Actemra™ tocilizumab	Genentech <i>South San Francisco, CA</i>	ankylosing spondylitis (see also rheumatoid arthritis)	Phase III (800) 626-3553
apremilast	Celgene <i>Summit, NJ</i>	ankylosing spondylitis (see also Behcet's syndrome, psoriatic arthritis, rheumatoid arthritis)	Phase II (908) 673-9000

SPONDYLITIS

Product Name	Company	Indication	Development Status
Arcoxia™ etoricoxib	Merck <i>Whitehouse Station, NJ</i>	ankylosing spondylitis (see also rheumatoid arthritis)	Phase III (800) 672-6372
Cimzia® certolizumab pegol	UCB <i>Smyrna, GA</i>	active axial spondyloarthritis (see also psoriatic arthritis)	Phase III (770) 970-7500
SAR153191 (anti-IL-6R mAb)	Regeneron Pharmaceuticals <i>Tarrytown, NY</i> sanofi-aventis <i>Bridgewater, NJ</i>	ankylosing spondylitis (see also rheumatoid arthritis)	Phase II (914) 345-7400 (800) 633-1610
secukinumab	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	ankylosing spondylitis (see also psoriatic arthritis, rheumatoid arthritis)	Phase I/II (888) 669-6682
tofacitinib (CP-690550)	Pfizer New York, NY	ankylosing spondylitis (see also psoriatic arthritis, rheumatoid arthritis)	Phase II (860) 732-5156

OTHER

Product Name	Company	Indication	Development Status
A-0001 (Orphan Drug)	Endo Pharmaceuticals <i>Chadd's Ford, PA</i>	Friedreich's ataxia	Phase II completed (613) 558-9800
AC-100	Acologix <i>Hayward, CA</i>	bone and cartilage disorders	Phase I (510) 512-7200
AMG 167	Amgen <i>Thousand Oaks, CA</i>	osteopenia	Phase I (800) 772-6436
AMG 785 (anti-sclerostin mAb)	Amgen <i>Thousand Oaks, CA</i>	fracture healing (see also osteoporosis)	Phase II (800) 772-6436
Benlysta® belimumab (intravenous)	GlaxoSmithKline <i>Rsch. Triangle Park, NC</i> Human Genome Sciences <i>Rockville, MD</i>	Sjögren's syndrome (see also lupus)	Phase II (888) 825-5249 (301) 309-8504
BioCart™ autologous cartilage system	BioChon Biotech <i>Woburn, MA</i>	cartilage lesions of the knee	Phase I (781) 305-5035
BMP-655 (PF-05208762)	Pfizer New York, NY	tendon injuries	Phase I (860) 732-5156
chondroitinase ABC	Seikagaku <i>Tokyo, Japan</i>	intervertebral disc displacement	Phase II www.seikagaku.co.jp
fibroblast growth factor-18	EMD Serono <i>Rockland, MA</i>	acute cartilage injury of the knee	Phase II (800) 283-8088
idebenone (Orphan Drug)	Santhera Pharmaceuticals <i>Charlestown, MA</i>	Friedreich's ataxia (Fast Track) (see also muscle disorders)	Phase III (617) 886-5161
juvenile chondrocyte grafts	ISTO Technologies <i>St. Louis, MO</i>	cartilage disorders	Phase I/II (314) 995-6049

OTHER

Product Name	Company	Indication	Development Status
KRN23	Kyowa Hakko Kirin America <i>Princeton, NJ</i>	X-linked dominant hypophosphataemic rickets	Phase I/II (609) 919-1100
LGD-4033	Ligand Pharmaceuticals <i>La Jolla, CA</i>	musculoskeletal disorders	Phase I (858) 550-7500
mesenchymal stem cell therapy	Mesoblast <i>New York, NY</i>	spinal fusion	Phase II (212) 880-2060
musculoskeletal mAb therapeutic	MorphoSys <i>Munich, Germany</i> Novartis Pharmaceuticals <i>East Hanover, NJ</i>	musculoskeletal disorders	Phase I www.morphosys.com (888) 669-6682
NeoCart [®] autologous chondrocyte implantation	Histogenics <i>Waltham, MA</i>	cartilage disorders	Phase III (781) 547-7900
OTI-030 (mesenchymal stem cell therapy)	Osiris Therapeutics <i>Columbia, MD</i>	knee injuries	Phase I/II (443) 545-1800
PL3100 (naproxen/ phosphatidylcholine)	PLx Pharma <i>Houston, TX</i>	arthritis	Phase II completed (713) 842-1249
RQ-00000005 (capromorelin)	RaQualia Pharma <i>Aichi, Japan</i>	frailty	Phase II www.raqualia.com
tissue repair stem cell therapy implant	Aastrom Biosciences <i>Ann Arbor, MI</i>	osteonecrosis	Phase III (734) 930-5555
		alveolar bone loss, non-union fracture, vertebral fracture	Phase I/II (734) 930-5555
Xgeva [™] denosumab	Amgen <i>Thousand Oaks, CA</i>	treatment-induced bone loss in patients with breast or prostate cancer	application submitted (800) 772-6436
Xiaflex [®] collagenase injection	Auxilium Pharmaceuticals <i>Malvern, PA</i>	frozen shoulder (parenteral)	Phase II (484) 321-5900
		tendon injuries (intramuscular)	Phase I (484) 321-5900

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 June 14, 2011.** The information in this report may not be comprehensive. For more specific information about a particular product, contact the individual company directly or go to www.clinicaltrials.gov. The entire series of *Medicines in Development* is available on PhRMA's web site.

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GLOSSARY

ankylosing spondylitis—An inflammatory disorder of unknown cause that primarily affects the spine. The vertebrae may fuse together and form a rigid back that is impossible to bend. The disorder may involve large joints, such as the hip.

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

Duchenne muscular dystrophy—An inherited disorder that involves rapidly worsening muscle weakness. Other muscular dystrophies get worse much more slowly. Duchenne muscular dystrophy is caused by a defective gene. Because of the way the disease is inherited, males are more likely to develop symptoms than are women.

fibromyalgia—Fibromyalgia syndromes are a group of disorders of unknown cause characterized by aching pain and stiffness in soft tissues, including muscles, tendons and ligaments. Fibromyalgia (pain and stiffness) may occur throughout the body or may be restricted to certain locations. A common variation, the primary fibromyalgia syndrome, usually occurs in previously healthy young women who may be depressed, anxious, or stressed, often with interrupted and nonrestorative sleep.

Friedreich's ataxia—An inherited disease that causes progressive damage to the nervous system resulting in symptoms ranging from gait disturbance and speech problems to heart disease. "Ataxia," which refers to coordination problems such as clumsy or awkward movements and unsteadiness, occurs in many different diseases and conditions.

gout—The pain of gout (called attacks or flares) is caused by inflammation when needle-like crystals are deposited in connective tissue and/or in the fluid that

cushions a joint (the synovial fluid). These crystals are made up of uric acid, a substance produced when the body breaks down purines found in human tissue and many foods we eat. Most uric acid is carried through the bloodstream to the kidneys, which eliminate it from the body in the urine. However, if the body produces too much uric acid or if the kidneys don't eliminate enough of it, uric acid can build up in the blood. An attack usually starts with sudden, severe pain, tenderness, redness, warmth, and swelling in the large joint of the big toe. After about 3-10 days, the attack usually subsides, and the next one may not happen for months or even years. But over time, the gout attacks can become more severe, last longer, affect more than one joint, and occur more often.

muscular atrophy—The wasting or loss of muscle tissue.

muscular spasticity—An abnormal increase in muscle tone. It may be associated with involuntary muscle spasms, sustained muscle contractions, and exaggerated deep tendon reflexes that make movement difficult or uncontrollable. Although it most commonly affects the legs and arms, spasticity can affect any part of the body including the trunk, neck, eyelids, face, or vocal cords.

osteoarthritis—The most common form of joint disease, characterized by degeneration of the cartilage that lines joints and by the formation of reactive bony outgrowths at the boundary of a joint.

osteonecrosis—Bone death caused by poor blood supply to the area, most commonly in the hip and shoulder. After a while, the bone can break off. If this condition is not treated, bone damage gets worse, and eventually, the affected part of the bone may collapse. Osteonecrosis can be caused by

disease, or a severe trauma, such as a break or dislocation, that affects the blood supply to the bone. Many times, no trauma or disease is present. That is called "idiopathic osteonecrosis," which means it occurs without any known cause.

osteopenia—Refers to bone mineral density (BMD) that is lower than normal peak BMD but not low enough to be classified as osteoporosis. Bone mineral density is a measurement of the level of minerals in the bones, which shows how dense and strong they are. Having osteopenia means there is a greater risk that, as time passes, you may develop osteoporosis.

osteoporosis—The most common metabolic bone disease in older people in which a reduction in bone mass leads to fractures, especially of the vertebrae, hips and wrists.

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 in humans.

Phase II—Effectiveness and safety testing in humans.

Phase III—Extensive clinical trials to demonstrate safety and efficacy in humans.

psoriatic arthritis—A type of chronic inflammatory arthritis associated with the chronic skin condition psoriasis, which is believed to be an inherited condition. Psoriatic arthritis typically appears about 10 years after the onset of psoriasis, which can manifest at any age, though most people are diagnosed between the ages of 15 and 35.

GLOSSARY

Raynaud's disease—A condition that causes some areas of the body—fingers, toes, the tip of the nose, and ears—to feel numb and cool in response to cold temperatures or stress. In Raynaud's disease, the smaller arteries that supply blood to the skin narrow, thus limiting blood circulation to affected areas.

rheumatoid arthritis—A type of arthritis that particularly attacks the small joints of the hands, wrists and feet. The joints become painful, swollen, stiff and, in severe cases, deformed.

scleroderma—A group of rare, progressive diseases that involve the hardening and tightening of the skin and connective tissues—the fibers that provide the framework and support for the body. Localized scleroderma affects only the skin. Systemic scleroderma also harms internal organs, such as the heart, lungs, kidneys, and digestive tract.

Sjögren's syndrome—A chronic autoimmune disease in which a person's white blood cells attack their moisture-producing glands. Although the hallmark symptoms

are dry eyes and dry mouth, Sjögren's may also cause dysfunction of other organs such as the kidneys, gastrointestinal system, blood vessels, lungs, liver, pancreas, and the central nervous system. Patients may also experience extreme fatigue and joint pain and have a higher risk of developing lymphoma.

systemic lupus erythematosus—A chronic autoimmune disorder, affecting many systems of the body, including the kidneys and brain.

SELECTED FACTS ABOUT MUSCULOSKELETAL DISORDERS AND ARTHRITIS

Overview¹

- Musculoskeletal disorders, including arthritis, encompasses more than 100 diseases and conditions that affect joints, the surrounding tissues, and other connective tissues. Approximately 46 million Americans have some type of arthritis or related condition, and 60 percent of them are female.
 - Arthritis-related disability is more prevalent among women than men at all ages: one in four women (24.4 percent) report having a disability compared with one in five men (19.1 percent). In absolute numbers, since 1999, there has been a 22 percent increase in the number of women who attribute their disability to arthritis (6.4 million).
 - The estimated cost of arthritis to the economy annually is some \$128 billion.
-

Behçet's Syndrome²

- **Behçet's disease**, an autoimmune disease that results from damage to blood vessels throughout the body, is common in the Middle East, Asia, and Japan. It is rare in the United States. In Middle Eastern and Asian countries, the disease affects more men than women. In the United States, it affects more women than men. Behçet's disease tends to develop in people in their 20's or 30's, but people of all ages can develop the disease.
-

Fibromyalgia³

- Fibromyalgia affects 3 million to 6 million Americans, up to 90 percent of whom are women. A recent study found that African-American women are more likely to suffer from fibromyalgia than their Caucasian counterparts.
-

Gout⁴

- **Gout**, a complex form of arthritis characterized by sudden, severe attacks of pain, redness and tenderness in joints, occurs more often in men than it does in women, primarily because women tend to have lower uric acid levels than men do. After menopause, however, women's uric acid levels approach those of men. 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.
-

Lupus⁵

- Anyone can get lupus, an inflammatory disease that may affect many parts of the body, but 9 out of 10 people who have lupus are women. African-American women are three times more likely to get lupus than white women. Lupus is also more common in Hispanic/Latina, Asian, and Native American women. African Americans and Hispanics/Latinos tend to get lupus at a younger age and have more symptoms, including kidney problems. Lupus also tends to be more severe in these ethnic groups. For example, African Americans with lupus have more problems with seizures and strokes. Hispanic/Latino patients have more heart problems.
-

Musculoskeletal Pain⁶

- Virtually all adults have experienced one or more brief episodes of **musculoskeletal pain** associated with injury or overuse. Recurrent or chronic musculoskeletal pain problems are also common. Although prevalence rates vary across studies of a given condition due to different case definitions, time periods, and populations studied, it is clear that the prevalence of certain musculoskeletal pain problems is fairly low (e.g., 2 percent or less for **fibromyalgia** and **rheumatoid arthritis**) whereas low back pain is extremely common, affecting up to 40 percent of adults in the general population at any given time. Prevalence is in the range of 15 percent to 20 percent for neck and shoulder pain and up to 15 percent for knee pain. The rates of many musculoskeletal pain problems vary greatly by age and sex. For example, knee pain from **osteoarthritis** is extremely common in the elderly, affecting more than one-third of people over age 60, but is much less common among younger people. Neck, shoulder, knee, and back pain are about 1.5 times more common in women than in men.

SELECTED FACTS ABOUT MUSCULOSKELETAL DISORDERS AND ARTHRITIS

Musculoskeletal Pain *(continued)*

- In a survey of the employed population in the United States, 7.2 percent of workers reported losing two or more hours of work in the past week due to back pain, **arthritis**, or other **musculoskeletal pain** conditions (including time spent at work without being productive due to pain). The mean time lost was 5 to 5.5 hours per week. The estimated total annual cost of productive time lost due to back pain, arthritis and other musculoskeletal pain problems was \$41.7 billion in 2002.
-

Osteoarthritis¹

- Osteoarthritis (OA), the most common form of arthritis, affects nearly 27 million Americans. Approximately 16 million OA sufferers are women, who usually develop the disorder after age 40.
-

Osteoporosis⁷

- Osteoporosis is a major public health threat for an estimated 44 million Americans, or 55 percent of people age 50 and older. Today, 10 million people already have the disease, 80 percent of whom are women. Another 34 million people have low bone density, placing them at increased risk for osteoporosis and broken bones.
 - In 2005, osteoporosis-related fractures were responsible for an estimated \$19 billion in costs. By 2025, experts predict that those costs will rise to approximately \$25.3 billion.
-

Psoriatic Arthritis⁸

- **Psoriatic arthritis**, a chronic disease characterized by inflammation of the skin (psoriasis) and joints (arthritis), is a common skin condition affecting 2 percent of the Caucasian population in the United States. Approximately 10 percent of patients who have psoriasis also develop an associated inflammation of their joints. The onset of psoriatic arthritis generally occurs in the fourth and fifth decades of life. Males and females are affected equally. The skin disease (psoriasis) and the joint disease (arthritis) often appear separately. In fact, the skin disease precedes the arthritis in nearly 80 percent of patients. However, the arthritis may precede the psoriasis in up to 15 percent of patients.
-

Raynaud's Disease⁴

- Raynaud's disease, a condition that causes some areas of the body to feel numb and cool in response to cold temperatures or stress, affects women more than men. Although anyone can develop the condition, primary Raynaud's often begins between the ages of 15 and 30. About one-third of people with primary Raynaud's have a first-degree relative—a parent, sibling or child—with the disorder.
-

Rheumatoid Arthritis¹

- Approximately 1.3 million American adults have rheumatoid arthritis (RA), with women outnumbering men 2.5-to-1. RA usually strikes women between the ages of 25 to 50.
 - Juvenile arthritis is one of the most common childhood diseases in the United States. Approximately 294,000 children under the age of 18 are affected by pediatric arthritis and rheumatologic conditions.
-

Scleroderma⁴

- Scleroderma, a group of rare, progressive diseases that causes hardening and tightening of the skin and connective tissues, occurs at least four times as often in women as it does in men and usually occurs between the ages of 30 and 50. Systemic scleroderma is more common in African Americans than it is in Americans of European descent, and those African-Americans are more likely to develop severe lung complications.⁷

SELECTED FACTS ABOUT MUSCULOSKELETAL DISORDERS AND ARTHRITIS

Sjögren's Syndrome⁹

- **Sjögren's syndrome** is one of the most prevalent autoimmune disorders, striking as many as 4 million Americans, of whom 9 out of 10 are women. About half of Sjögren's cases occur along with another connective tissue disease, primarily **rheumatoid arthritis**, **systemic lupus**, and **scleroderma**.
-

Spondylitis⁸

- **Ankylosing spondylitis**, a form of chronic inflammation of the spine and the sacroiliac joints, is two to three times more common in males than in females. In women, joints away from the spine are more frequently affected than in men. Ankylosing spondylitis affects all age groups, including children. The most common age of onset of symptoms is in the second and third decades of life.
-

Sources:

1. Arthritis Foundation (www.arthritis.org)
 2. American Behcet's Disease Association (www.behcets.com)
 3. www.Fibromyalgia-Symptoms.org
 4. Mayo Foundation for Medical Education and Research (www.mayoclinic.com)
 5. Office on Women's Health, U.S. Department of Health and Human Services (www.womenshealth.gov)
 6. International Association for the Study of Pain (www.iasp-pain.org)
 7. National Osteoporosis Foundation (www.nof.org)
 8. MedicineNet, Inc. (www.medicinenet.com)
 9. Sjogren's Syndrome Foundation (www.sjogrens.org)
-

Note:

Cover quote from John Howard Klippel, MD (www.arthritis.org/top-10-advances-2008.php)

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 \$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.

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 21 new therapeutics approved by the FDA in 2010 was 14.8 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 \$67.4 billion in research and development in 2010.

TRACKING THE BIOPHARMACEUTICAL RESEARCH PIPELINE

Today, more than 3,000 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 biopharmaceutical research pipeline 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 2011 report found 887 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 2011 report found 299 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 the pipeline.*
- **Infectious Diseases**—Throughout history, infectious diseases have taken a devastating toll on the lives and well-being of people around the world. Today, vaccines and antibiotics have proven to be effective treatments in many cases, but infectious diseases still pose a very serious threat to patients. Infectious diseases may never be eradicated. But, new knowledge, new technologies, and a huge commitment of resources by America's biopharmaceutical research companies and the government can help meet the continuing—and ever-changing—threat from infectious diseases. *The 2010 report found 395 medicines in the pipeline.*



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