

2015 Medicines in Development for Heart Disease and Stroke

A Report on Cardiovascular Disease

Acute Coronary Syndrome

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
apabetalone/RVX-208 (BET protein inhibitor)	Resverlogix <i>Calgary, Canada</i>	acute coronary syndrome (see also <i>atherosclerosis</i>)	Phase II completed www.resverlogix.com
CER-001 (apolipoprotein A1 stimulant)	Cerenis Therapeutics <i>Ann Arbor, MI</i>	post-acute coronary syndrome (see also <i>lipid disorders</i>)	Phase II www.cerenis.com
losmapimod (p38 kinase inhibitor)	GlaxoSmithKline <i>Research Triangle Park, NC</i>	acute coronary syndrome	Phase III www.gsk.com
MEDI6012 (recombinant LCAT)	MedImmune <i>Gaithersburg, MD</i>	acute coronary syndrome	Phase I www.medimmune.com
PF-06282999	Pfizer <i>New York, NY</i>	acute coronary syndrome	Phase I www.pfizer.com
Vytorin [®] ezetimibe/simvastatin	Merck <i>Kenilworth, NJ</i>	acute coronary syndrome	Phase III completed www.merck.com
Xarelto [®] rivaroxaban	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i> Janssen Research & Development <i>Raritan, NJ</i>	acute coronary syndrome (secondary prevention) (Fast Track) (see also <i>coronary artery disease, heart failure, peripheral vascular disease, stroke, thrombosis</i>)	application submitted www.pharma.bayer.com www.janssenrnd.com
Zetia [®] ezetimibe	Merck <i>Kenilworth, NJ</i>	acute coronary syndrome	Phase III completed www.merck.com

Adjunctive Therapies

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
andexanet alfa (factor Xa inhibitor antidote) ORPHAN DRUG	Portola Pharmaceuticals <i>South San Francisco, CA</i>	anticoagulant reversal	Phase III www.portola.com
ATryn® recombinant antithrombin alfa ORPHAN DRUG	rEVO Biologics <i>Framingham, MA</i>	heparin resistance in patients undergoing coronary artery bypass graft (CABG) <i>(see also hypertension)</i>	Phase III www.revobiologics.com
		heparin resistance in neonates undergoing CABG	Phase I www.revobiologics.com
bivalirudin (ready-to-use)	Eagle Pharmaceuticals <i>Woodcliff Lake, NJ</i>	heparin-induced thrombocytopenia and thrombosis syndrome in patients undergoing percutaneous coronary intervention, unstable angina in patients undergoing percutaneous transluminal coronary angioplasty	application submitted www.eagleus.com
ciraparantag (factor Xa inhibitor)	Perosphere <i>Danbury, CT</i>	anticoagulant reversal (Fast Track)	Phase II www.perosphere.com
CMX-2043 (proto-oncogene protein C AKT modulator)	Ischemix <i>Maynard, MA</i>	prevention of ischemia-reperfusion injury in patients undergoing percutaneous coronary intervention (PCI)	Phase II www.ischemix.com
LB1148 (tranexamic acid)	Leading BioSciences <i>Solana Beach, CA</i>	prevention of cardiogenic shock following cardiovascular surgery	Phase II www.leadingbiosciences.com
MABp1 (IL-1 alpha inhibitor)	XBiotech <i>Austin, TX</i>	prevention of vascular restenosis in percutaneous, superficial femoro-popliteal revascularization (Fast Track)	Phase II www.xbiotech.com

Arrhythmia/Atrial Fibrillation

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
dronedarone/ranolazine fixed-dose combination	Gilead Sciences <i>Foster City, CA</i>	paroxysmal atrial fibrillation	Phase II completed www.gilead.com
eleclazine (late sodium current inhibitor)	Gilead Sciences <i>Foster City, CA</i>	long QT-3 syndrome (see also cardiomyopathy)	Phase III www.gilead.com
		ventricular tachycardia/ventricular fibrillation	Phase II www.gilead.com
Gencaro™ bucindolol	ARCA biopharma <i>Westminster, CO</i>	atrial fibrillation (prevention) (Fast Track)	Phase II/III www.arcabiopharma.com
IKur inhibitor	Bristol-Myers Squibb <i>Princeton, NJ</i>	atrial fibrillation	Phase II www.bms.com
MSP-2017 (calcium channel antagonist)	Milestone Pharmaceuticals <i>Quebec, Canada</i>	paroxysmal supraventricular tachycardia	Phase II www.milestonepharma.com
OPC-108459	Otsuka America Pharmaceutical <i>Rockville, MD</i>	paroxysmal and persistent atrial fibrillation	Phase I www.otsuka.com
vanoxerine (dopamine re-uptake inhibitor)	Laguna Pharmaceuticals <i>La Jolla, CA</i>	atrial fibrillation	Phase III www.lagunarx.com
vernakalant (oral)	Cardiome Pharma <i>Vancouver, Canada</i>	atrial fibrillation	Phase II www.cardiome.com

Atherosclerosis

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
AHRO-001 (cholesterol absorption inhibitor)	AtheroNova <i>Irvine, CA</i>	atherosclerosis	Phase I www.atheronova.com

Atherosclerosis

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
anacetrapib (cholesterol ester transfer protein inhibitor)	Merck <i>Kenilworth, NJ</i>	atherosclerosis (see also lipid disorders)	Phase III www.merck.com
apabetalone/RVX-208 (BET protein inhibitor)	Resverlogix <i>Calgary, Canada</i>	atherosclerosis (see also acute coronary syndrome)	Phase II completed www.resverlogix.com
canakinumab (ACZ885)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	atherosclerosis (secondary prevention of cardiovascular events)	Phase III www.novartis.com
CSL-112 (cholesterol modulator)	CSL <i>Victoria, Australia</i>	atherosclerosis (see also heart attack)	Phase II www.csl.com.au
K-134 (PDE3 inhibitor)	Kowa Research Institute <i>Morrisville, NC</i>	arteriosclerotic disease	Phase II www.kowaus.com
MLN1202 (CCR2 receptor antagonist)	Takeda Pharmaceuticals <i>Deerfield, IL</i>	atherosclerosis	Phase II www.takeda.com
PVT-100 (eicosapentaenoic/docosahexaenoic)	Pivotal Therapeutics <i>Boca Raton, FL</i>	atherosclerosis (stabilization of plaque)	Phase II www.pivotaltherapeutics.us
VB-201 (anti-inflammatory)	VBL Therapeutics <i>Or Yehuda, Israel</i>	atherosclerosis	Phase II www.vblrx.com

Cardiomyopathy

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
ARRY-797 (P38 mitogen-activated protein kinase inhibitor)	Array BioPharma <i>Boulder, CO</i>	lamin A/C-related dilated cardiomyopathy	Phase II www.arraybiopharma.com

Cardiomyopathy

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
eleclazine (late sodium current inhibitor)	Gilead Sciences <i>Foster City, CA</i>	hypertrophic cardiomyopathy (see also <i>arrhythmia</i>)	Phase II www.gilead.com
ixmyelocel-T (cell replacement therapy) ORPHAN DRUG	Vericel <i>Cambridge, MA</i>	ischemic dilated cardiomyopathy	Phase II completed www.vcel.com
MEK162 (MAP kinase 1/2 inhibitor)	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	hypertrophic cardiomyopathy	Phase II www.novartis.com
MYK-461/SAR439152 (myosin modulator)	MyoKardia <i>South San Francisco, CA</i> Sanofi <i>Bridgewater, NJ</i>	hypertrophic cardiomyopathy	Phase I www.myokardia.com www.sanofi.com
revusiran (ALN-TTRSC) (siRNA inhibitor) ORPHAN DRUG	Alnylam Pharmaceuticals <i>Cambridge, MA</i> Genzyme <i>Cambridge, MA</i>	familial amyloid cardiomyopathy	Phase III www.alnylam.com
Vyndaqel™ tafamidis meglumine ORPHAN DRUG	Pfizer <i>New York, NY</i>	adult symptomatic transthyretin cardiomyopathy	Phase III www.pfizer.com

Coronary Artery Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
autologous stem cell therapy	Baxalta <i>Bannockburn, IL</i>	chronic myocardial ischemia	Phase III www.baxalta.com
Brilinta® ticagrelor	AstraZeneca <i>Wilmington, DE</i>	coronary artery disease in patients with type 2 diabetes (see also <i>peripheral vascular disease, stroke</i>)	Phase III www.astrazeneca.com

Coronary Artery Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Combo™ Dual Therapy Stent anti-CD34 antibody-coated sirolimus-eluting stent	OrbusNeich <i>Ft. Lauderdale, FL</i>	coronary artery disease (restenosis prevention)	Phase II/III
CVBT-141 (fibroblast growth factor 1)	CardioVascular BioTherapeutics <i>Las Vegas, NV</i>	severe coronary heart disease (see also peripheral vascular disease)	Phase II www.cvbt.com
Generx® alferminogene tadenovec	Taxus Cardium Pharmaceuticals <i>San Diego, CA</i>	cardiac microvascular insufficiency in advanced coronary artery disease (Fast Track)	Phase III www.cardiumtx.com
MDCO-216 (apolipoprotein A I stimulant)	The Medicines Company <i>Parsippany, NJ</i>	coronary artery disease	Phase I www.themedicinescompany.com
myolimus-eluting biodegradable stent	Elixir Medical <i>Sunnyvale, CA</i>	coronary artery disease (restenosis prevention)	Phase I www.elixirmedical.com
ridaforolimus-eluting coronary stent	Medinol USA <i>Parsippany, NJ</i>	coronary artery disease (restenosis prevention)	Phase II www.medinol.com
sirolimus-eluting coronary stent	REVA Medical <i>San Diego, CA</i>	coronary artery disease	in clinical trials www.teamreva.com
sirolimus-eluting coronary stent	Svelte Medical Systems <i>New Providence, RI</i>	coronary artery disease	Phase II www.sveltemedical.com
umiroliimus-eluting stent (sirolimus analogue)	Biosensors International <i>Singapore</i>	coronary artery disease	Phase II/III www.biosensors.com
Xarelto® rivaroxaban	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i> Janssen Research & Development <i>Raritan, NJ</i>	reduction of major adverse cardiac events (MACE) in patients with significant coronary artery disease (see also acute coronary syndrome, heart failure, peripheral vascular disease, stroke, thrombosis)	Phase III www.pharma.bayer.com www.janssenrnd.com

Heart Attack Product Name	Sponsor	Indication	Development Status
CAP-1002 (allogeneic cardiosphere-derived stem cell therapeutic)	Capricor Therapeutics <i>Beverly Hills, CA</i>	post myocardial infarction (see also heart failure)	Phase II www.capricor.com
CLBS10 (cell replacement therapy)	Caladrius Biosciences <i>Basking Ridge, NJ</i>	ST-elevation myocardial infarction (STEMI)	Phase II www.calarius.com
CSL-112 (cholesterol modulator)	CSL <i>Victoria, Australia</i>	acute myocardial infarction (see also atherosclerosis)	Phase II www.csl.com.au
MultiStem [®] allogeneic stem cell therapy	Athersys <i>Cleveland, OH</i>	acute myocardial infarction (see also stroke)	Phase II www.athersys.com
Prochymal [®] remestemcel-L	Mesoblast <i>New York, NY</i>	myocardial infarction	Phase II www.mesoblast.com
rexlemestrocel-L (mesenchymal precursor stem cells)	Mesoblast <i>New York, NY</i> Teva Pharmaceuticals USA <i>North Wales, PA</i>	myocardial infarction (see also heart failure)	Phase II www.mesoblast.com www.tevapharm.com
RGN-351 injectable (thymosin-beta 4)	RegeneRx Biopharmaceuticals <i>Rockville, MD</i>	acute myocardial infarction	Phase I completed www.regenerx.com
RNS60 (charge-stabilized nanostructure saline product)	Revalesio <i>Tacoma, WA</i>	acute myocardial infarction	Phase I www.revalesio.com
sodium nitrate	Hope Pharmaceuticals <i>Scottsdale, AZ</i>	acute myocardial infarction (see also stroke)	Phase II www.hopepharm.com
Stemedyne [™] -MSC mesenchymal stem cell therapy	Semedica Cell Technologies <i>San Diego, CA</i>	STEMI (see also heart failure, stroke)	Phase II www.stemedica.com

Heart Failure
Product Name

Sponsor

Indication

Development Status

AdipoCell™ adipose-derived autologous stem cell therapy	Bioheart <i>Sunrise, FL</i>	congestive heart failure	Phase I/II www.bioheartinc.com
AIR001 (sodium nitrite inhalation)	Mast Therapeutics <i>San Diego, CA</i>	heart failure with preserved ejection fraction	Phase II www.masttherapeutics.com
ANX-042 (natriuretic peptide)	Anexon <i>Cambridge, MA</i>	acute decompensated heart failure	Phase I completed www.anexonrx.com
BAY 1067197 (partial adenosine A1 agonist)	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i>	chronic heart failure	Phase II www.pharma.bayer.com
BAY 1142524 (chymase inhibitor)	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i>	heart failure (elderly)	Phase II www.pharma.bayer.com
Bendavia™ mitochondrial permeability transition pore inhibitor	Stealth BioTherapeutics <i>Newton, MA</i>	heart failure	Phase II www.stealthbt.com
BiDil XR™ hydralazine/isosorbide dinitrate extended release	Arbor Pharmaceuticals <i>Atlanta, GA</i>	heart failure	Phase I/II www.arborpharma.com
CAP-1002 (allogeneic cardiosphere-derived stem cell therapeutic)	Capricor Therapeutics <i>Beverly Hills, CA</i>	heart failure <i>(see also heart attack)</i>	Phase I/II www.capricor.com
CardiALLO™ allogeneic culture expanded mesenchymal stem cells derived from bone marrow	Biocardia <i>San Carlos, CA</i>	heart failure	Phase I completed www.biocardia.com

Heart Failure
Product Name

Sponsor

Indication

Development Status

CardiAMP™ autologous minimally processed bone marrow cells	Biocardia <i>San Carlos, CA</i>	heart failure	Phase II completed www.biocardia.com
cenderitide (natriuretic peptide)	Capricor Therapeutics <i>Beverly Hills, CA</i>	acute decompensated heart failure (Fast Track), chronic heart failure (Fast Track)	Phase II www.capricor.com
cimaglermin alfa (glial growth factor 2)	Acorda Therapeutics <i>Ardsley, NY</i>	congestive heart failure (Fast Track)	Phase I www.acorda.com
CLP-1001 (sodium potassium chloride symporter inhibitor)	Sorbent Therapeutics <i>Sunnyvale, CA</i>	congestive heart failure	Phase II
CXL-1427 (nitroxyl donor therapeutic)	Cardioxyl Pharmaceuticals <i>Chapel Hill, NC</i>	acute decompensated heart failure	Phase II www.cardioxyl.com
finerenone (MR antagonist)	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i>	chronic heart failure	Phase III www.pharma.bayer.com
furosemide subcutaneous	scPharmaceuticals <i>Lexington, MA</i>	chronic heart failure	Phase II/III www.scpharmaceuticals.com
GSK2798745 (TRPV4 antagonist)	GlaxoSmithKline <i>Research Triangle Park, NC</i>	heart failure	Phase I www.gsk.com
JVS-100 (non-viral gene therapy)	Juventas Therapeutics <i>Cleveland, OH</i>	heart failure (Fast Track) <i>(see also peripheral vascular disease)</i>	Phase II www.juventasinc.com
MyoCell™ muscle-derived autologous stem cell therapy	Bioheart <i>Sunrise, FL</i>	heart failure	Phase II/III www.bioheartinc.com

Heart Failure Product Name	Sponsor	Indication	Development Status
omecamtiv mecarbil (cardiac myosin activator)	Amgen Thousand Oaks, CA Cytokinetics South San Francisco, CA	heart failure	Phase II www.amgen.com www.cytokinetics.com
ONO-4232 (prostaglandin E EP4 receptor agonist)	Ono Pharma USA Trenton, NJ	acute heart failure	Phase I www.ono.co.jp
PL-3994 (natriuretic peptide receptor A agonist)	Palatin Technologies Cranbury, NJ	heart failure	Phase II www.palatin.com
recombinant human neuregulin-1 beta	Zensun USA San Diego, CA	chronic heart failure	Phase II completed www.zensunusa.com
rexlemestrocel-L (mesenchymal precursor stem cells)	Mesoblast New York, NY Teva Pharmaceuticals USA North Wales, PA	class II/III congestive heart failure (see also heart attack)	Phase III www.mesoblast.com www.tevapharm.com
		end-stage congestive heart failure	Phase II www.mesoblast.com www.tevapharm.com
RT-100 (Ad5.hAC6 gene therapy)	Renova Therapeutics San Diego, CA	congestive heart failure	Phase I/II www.renovatherapeutics.com
serelaxin (recombinant human relaxin)	Novartis Pharmaceuticals East Hanover, NJ	acute heart failure (Fast Track) (adjunctive treatment)	application submitted www.novartis.com
		acute heart failure (pediatrics), chronic heart failure	Phase II www.novartis.com
Stemedyne™-MSC mesenchymal stem cell therapy	Semedica Cell Technologies San Diego, CA	chronic heart failure (see also heart attack, stroke)	Phase II www.stemedica.com

Heart Failure
Product Name

Sponsor

Indication

Development Status

Tekturna®
aliskiren

Novartis Pharmaceuticals
East Hanover, NJ

reduction of cardiovascular death
and hospitalization in chronic heart failure
(*see also hypertension*)

Phase III
www.novartis.com

TRV027
(angiotensin II type 1 receptor
antagonist)

Allergan
Parsippany, NJ
Trevena
King of Prussia, PA

acute heart failure

Phase II
www.allergan.com
www.trevenainc.com

ularitide
(atrial peptide agonist)

Cardioentis
Zug, Switzerland

acute decompensated heart failure

Phase III
www.cardioentis.com

vepoloxamer (MST-188)
(cell membrane structure modulator)

Mast Therapeutics
San Diego, CA

chronic heart failure
(*see also peripheral vascular disease*)

Phase II
www.masttherapeutics.com

vericiguat
(sGC stimulator)

Bayer HealthCare Pharmaceuticals
Whippany, NJ
Merck
Kenilworth, NJ

worsening chronic heart failure

Phase II
www.pharma.bayer.com
www.merck.com

Xarelto®
rivaroxaban

Bayer HealthCare Pharmaceuticals
Whippany, NJ
Janssen Research & Development
Raritan, NJ

reduction of MACE in patients with chronic
heart failure
(*see also acute coronary syndrome, coronary
artery disease, peripheral vascular disease,
stroke, thrombosis*)

Phase III
www.pharma.bayer.com
www.janssenrnd.com

Hypertension
Product Name

Sponsor

Indication

Development Status

ATryn®
recombinant antithrombin alfa

rEVO Biologics
Framingham, MA

preeclampsia
(*see also adjunctive therapies*)

Phase III
www.revobiologics.com

Hypertension
Product Name

Sponsor

Indication

Development Status

candesartan cilexetil/nifedipine fixed dose combination (angiotensin type 1 receptor antagonist/calcium channel antagonist)	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i>	essential hypertension	Phase III www.pharma.bayer.com
DigiBind [®] anti-digoxin polyclonal antibody ORPHAN DRUG	Glenveigh Medical <i>Chattanooga, TN</i>	preeclampsia (Fast Track)	Phase II www.glenveigh.com
Edarbi [®] azilsartan medoxomil	Arbor Pharmaceuticals <i>Atlanta, GA</i>	hypertension (pediatric)	Phase III www.arborpharma.com
Entresto [™] sacubitril/valsartan	Novartis Pharmaceuticals <i>East Hanover, NJ</i>	hypertension	Phase II www.novartis.com
HL-040XC (atorvastatin/losartan fixed-dose combination)	HanAll Biopharma <i>Seoul, South Korea</i>	hypertension (see also lipid disorders)	Phase II www.hanall.co.kr
KIT-301 (naproxen/anti-hypertensive fixed-dose combination)	Kitov Pharmaceuticals <i>Washington, DC</i>	high blood pressure caused by NSAID use	in clinical trials www.kitovpharma.com
neбиволол/valsartan fixed-dose combination	Allergan <i>Parsippany, NJ</i>	essential hypertension	application submitted www.allergan.com
PB1046 (vasoactive intestinal peptide type II receptor agonist)	PhaseBio Pharmaceuticals <i>Malvern, PA</i>	essential hypertension	Phase I www.phasebio.com
sGC stimulator	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i>	hypertension	Phase I www.pharma.bayer.com

Hypertension
Product Name

Sponsor

Indication

Development Status

Tekturna®
aliskiren

Novartis Pharmaceuticals
East Hanover, NJ

hypertension (pediatric)
(see also heart failure)

Phase III
www.novartis.com

Uloric®
febuxostat

Takeda Pharmaceuticals
Deerfield, IL

lower ambulatory blood pressure in hypertension
and hyperuricemia not associated with gout

Phase II completed
www.takeda.com

Lipid Disorders
Product Name

Sponsor

Indication

Development Status

AEM-28
(apolipoprotein B modulator)
ORPHAN DRUG

Capstone Therapeutics
Tempe, AZ
Lipimetix
Natick, MA

hypercholesterolemia,
hyperlipoproteinemia type IIa

Phase II
www.capstonethx.com
www.lipimetix.com

ALN-PCS
(PCSK9 protein inhibitor)

Alnylam Pharmaceuticals
Cambridge, MA
The Medicines Company
Parsippany, NJ

hypercholesterolemia

Phase I
www.alnylam.com
www.themedicinescompany.com

AMR101
(ethyl eicosapentaenoic acid)

Amarin Pharma
Dublin, Ireland

hypertriglyceridemia

Phase III
www.amarincorp.com

anacetrapib
(cholesterol ester transfer
protein inhibitor)

Merck
Kenilworth, NJ

heterozygous familial hypercholesterolemia,
hypercholesterolemia
(see also atherosclerosis)

Phase III
www.merck.com

ARI-3037MO
(niacin analog)

Arisaph Pharmaceuticals
Boston, MA

dyslipidemia, hypertriglyceridemia

Phase II
www.arisaph.com

bococizumab
(PCSK9 inhibitor)

Pfizer
New York, NY

hyperlipidemia

Phase III
www.pfizer.com

CAT-2003
(eicosapentaenoic acid/niacin)

Catabasis Pharmaceuticals
Cambridge, MA

hypertriglyceridemia

Phase II
www.catabasis.com

Lipid Disorders

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
CAT-2054 (icosapentaenoic acid/niacin)	Catabasis Pharmaceuticals <i>Cambridge, MA</i>	hypercholesterolemia	Phase II www.catabasis.com
CER-001 (apolipoprotein A1 stimulant)	Cerenis Therapeutics <i>Ann Arbor, MI</i>	familial HDL-cholesterol deficiency (see also acute coronary syndrome)	Phase II www.cerenis.com
Epanova [®] omega-3 carboxylic acids	AstraZeneca <i>Wilmington, DE</i>	persistent hypertriglyceridemia plus low HDL cholesterol	Phase III www.astrazeneca.com
ETC-1002 (peroxisome proliferator-activated receptor agonist)	Esperion Therapeutics <i>Ann Arbor, MI</i>	hypercholesterolemia (LDL-cholesterol lowering)	Phase II www.esperion.com
Glybera [®] alipogene tiparovec ORPHAN DRUG	UniQure <i>Lexington, MA</i>	hyperlipoproteinemia type I	Phase III www.uniqure.com
HL-040XC (atorvastatin/losartan fixed-dose combination)	HanAll Biopharma <i>Seoul, South Korea</i>	hyperlipidemia (see also hypertension)	Phase II www.hanall.co.kr
icosabutate (omega-3 fatty acid icosapentaenoic acid)	BASF <i>Oslo, Norway</i>	severe hypertriglyceridemia	Phase II www.omega3.basf.com
ISIS-ANGPTL3-L _{Rx} (antisense angiopoietin-like 3 protein inhibitor)	Akcea Therapeutics <i>Cambridge, MA</i>	mixed dyslipidemia	Phase I www.akceatx.com
ISIS-APO(a) _{Rx} (apolipoprotein A inhibitor)	Akcea Therapeutics <i>Cambridge, MA</i>	recurrent cardiovascular events with high lipoprotein(a)	Phase II www.akceatx.com
ISIS-APO(a)-L _{Rx} (apolipoprotein A inhibitor)	Akcea Therapeutics <i>Cambridge, MA</i>	recurrent cardiovascular events with high lipoprotein(a)	Phase I www.akceatx.com

Lipid Disorders

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
K-312 (PCSK9 protein inhibitor)	Kowa Research Institute <i>Morrisville, NC</i>	dyslipidemia	Phase I www.kowaus.com
K-877 (PPAR-alpha agonist)	Kowa Research Institute <i>Morrisville, NC</i>	dyslipidemia	Phase II www.kowaus.com
LY3015014 (PCSK9 MAb)	Eli Lilly <i>Indianapolis, IN</i>	hypercholesterolemia	Phase II www.lilly.com
MAT-9001 (triglyceride modulator)	Matinas BioPharma <i>Bedminster, NJ</i>	hypertriglyceridemia	Phase I www.matinasbiopharma.com
MBX-8025 (PPAR-delta agonist)	CymaBay Therapeutics <i>Newark, CA</i>	hyperlipidemia	Phase II www.cymbay.com
MGL-3196 (thyroid hormone receptor agonist)	Madrigal Pharmaceuticals <i>Fort Washington, PA</i>	dyslipidemia, hypercholesterolemia	Phase I www.madrigalpharma.com
PF-06427878	Pfizer <i>New York, NY</i>	hyperlipidemia	Phase I www.pfizer.com
Praluent [®] alirocumab	Regeneron Pharmaceuticals <i>Tarrytown, NY</i> Sanofi US <i>Bridgewater, NJ</i>	heterozygous familial hypercholesterolemia	Phase III www.regeneron.com www.sanofi.com
rosuvastatin zinc (HMG-CoA reductase inhibitor)	Allergan <i>Parsippany, NJ</i>	hypertriglyceridemia	application submitted www.allergan.com
TP-452 (eicosapentaenoic/metformin)	Thetis Pharmaceuticals <i>Southport, CT</i>	control of LDL-cholesterol, mixed dyslipidemia	Phase I www.thetispharma.com

Lipid Disorders

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
VK2809 (thyroid hormone receptor beta agonist)	Viking Therapeutics <i>San Diego, CA</i>	hypercholesterolemia	Phase I www.vikingtherapeutics.com

volanesorsen (apolipoprotein C-III inhibitor)	Akcea Therapeutics <i>Cambridge, MA</i>	familial chylomicronemia syndrome, hypertriglyceridemia	Phase III www.akceatx.com
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Peripheral Vascular Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
ACY001 (autologous AC133+selected adult bone marrow-derived stem cell therapy)	Arterioocyte <i>Cleveland, OH</i> Compass Biomedical <i>Cleveland, OH</i>	peripheral vascular disease with critical limb ischemia	Phase I www.arterioocyte.com

ALD-301 (adult stem cell therapy)	Aldagen <i>Durham, NC</i>	peripheral arterial occlusive disorder with intermittent claudication	Phase II
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autologous stem cell therapy	Lifecells <i>Irvine, CA</i>	critical limb ischemia	Phase I/II www.lifecellsllc.com
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Brilinta [®] ticagrelor	AstraZeneca <i>Wilmington, DE</i>	peripheral artery disease (see also coronary artery disease, stroke)	Phase III www.astrazeneca.com
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Collatogene [®] beperminogene perplasmid (HGF plasmid)	AnGes <i>Bethesda, MD</i>	critical limb ischemia (Fast Track)	Phase III www.anges-mg.com
		ischemic heart disorders	Phase I completed www.anges-mg.com

CVBT-141 (fibroblast growth factor 1)	CardioVascular BioTherapeutics <i>Las Vegas, NV</i>	peripheral artery disease (see also coronary artery disease)	Phase II www.cvbt.com
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Peripheral Vascular Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
human plasma-derived fibrinolysin ORPHAN DRUG	Grifols Therapeutics <i>Barcelona, Spain</i>	acute peripheral arterial occlusion	Phase II www.grifols.com
JVS-100 (non-viral gene therapy)	Juventas Therapeutics <i>Cleveland, OH</i>	critical limb ischemia (see also heart failure)	Phase II www.juventasinc.com
MDT-2113 (paclitaxel-coated angioplasty balloon)	Medtronic Endovascular <i>Minneapolis, MN</i>	peripheral arterial occlusive disorder	Phase II www.medtronicendovascular.com
MultiGeneAngio cell therapy	MultiGene Vascular Systems <i>Haifa, Israel</i>	peripheral artery disease	Phase I/II www.mgvs.co.il
paclitaxel-eluting bioresorbable scaffold	480 Biomedical <i>Watertown, MA</i>	peripheral artery disease	Phase II www.480biomedical.com
PDA-002 (cell therapy)	Celgene <i>Summit, NJ</i>	peripheral artery disease	Phase II www.celgene.com
PLX-PAD (stromal cell therapy)	Pluristem Therapeutics <i>Haifa, Israel</i> United Therapeutics <i>Research Triangle Park, NC</i>	intermittent claudication	Phase II www.pluristem.com www.unither.com
		critical limb ischemia	Phase I www.pluristem.com www.unither.com
TV-1001 (sodium nitrite oral)	Theravasc <i>Cleveland, OH</i>	peripheral artery disease	Phase II www.thervasc.com
vepoloxamer (MST-188) (cell membrane structure modulator)	Mast Therapeutics <i>San Diego, CA</i>	peripheral arterial occlusive disorders (see also heart failure)	Phase II www.masttherapeutics.com

Peripheral Vascular Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
VM202 (modified hepatocyte growth factor gene therapy)	ViroMed <i>Seoul, South Korea</i>	critical limb ischemia	Phase II www.viromed.co.kr
vonapanitase (recombinant human elastase)	Proteon Therapeutics <i>Waltham, MA</i>	peripheral arterial disease	Phase I www.proteontherapeutics.com
Xarelto® rivaroxaban	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i> Janssen Research & Development <i>Raritan, NJ</i>	reduction of MACE in patients with peripheral arterial disease <i>(see also acute coronary syndrome, coronary artery disease, heart failure, stroke, thrombosis)</i>	Phase III www.pharma.bayer.com www.janssenrnd.com

Pulmonary Vascular Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Adcirca™ tadalafil	Eli Lilly <i>Indianapolis, IN</i>	pulmonary arterial hypertension (pediatric)	Phase III www.lilly.com
Adempas® riociguat ORPHAN DRUG	Bayer HealthCare Pharmaceuticals <i>Whippany, NJ</i>	pulmonary hypertension (combination therapy)	Phase II www.pharma.bayer.com
bardoxolone methyl ORPHAN DRUG	Reata Pharmaceuticals <i>Irving, TX</i>	pulmonary arterial hypertension	Phase II www.reatapharm.com
beraprost 314d modified release	Lung Biotechnology <i>Silver Spring, MD</i>	pulmonary arterial hypertension	Phase III www.lungbiotechnology.com
GS-4997 (ASK-1 inhibitor)	Gilead Sciences <i>Foster City, CA</i>	pulmonary arterial hypertension	Phase II www.gilead.com
INOpulse® nitric acid inhalation ORPHAN DRUG	Bellerophon Therapeutics <i>Warren, NJ</i>	pulmonary arterial hypertension	Phase III www.bellerophon.com

Pulmonary Vascular Disease

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Opsumit® macitentan	Actelion Pharmaceuticals <i>South San Francisco, CA</i>	inoperable chronic thromboembolic pulmonary hypertension combined pre- and post-capillary pulmonary hypertension <i>(see also other)</i>	Phase II www.actelion.com
orenitram® treprostinil oral	United Therapeutics <i>Silver Spring, MD</i>	pulmonary arterial hypertension (pediatric)	Phase II www.unither.com
ralinepag ORPHAN DRUG	Arena Pharmaceuticals <i>San Diego, CA</i>	pulmonary arterial hypertension	Phase II www.arenapharm.com
Remodulin® treprostinil injection	United Therapeutics <i>Silver Spring, MD</i>	pulmonary arterial hypertension (neonates)	Phase II www.unither.com
Revatio® sildenafil intravenous	Pfizer <i>New York, NY</i>	persistent pulmonary arterial hypertension (neonates)	Phase III www.pfizer.com
selexipag (epoprostenol receptor agonist)	Actelion Pharmaceuticals <i>South San Francisco, CA</i>	pulmonary arterial hypertension	application submitted www.actelion.com
SPI-026 (tacrolimus)	Selten Pharma <i>Saratoga, CA</i>	pulmonary arterial hypertension	Phase II www.seltenpharma.com
SPI-183	Selten Pharma <i>Saratoga, CA</i>	pulmonary arterial hypertension	Phase I www.seltenpharma.com

Stroke

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
3K3A-APC (recombinant mutant wild-type activated protein C)	ZZ Biotech <i>Houston, TX</i>	acute ischemic stroke	Phase II www.zzbiotech.com

Stroke Product Name	Sponsor	Indication	Development Status
Brilinta® ticagrelor	AstraZeneca <i>Wilmington, DE</i>	reduction of vascular events in acute ischemic stroke or transient ischemic attack <i>(see also coronary artery disease, peripheral vascular disease)</i>	Phase III www.astrazeneca.com
Cirara™ glibenclamide	Remedy Pharmaceuticals <i>New York, NY</i>	severe ischemic stroke	Phase II www.remedypharmaceuticals.com
dalfampridine	Acorda Therapeutics <i>Ardsley, NY</i>	chronic post-stroke walking deficits	Phase III www.acorda.com
DS-1040 (TAFIa inhibitor)	Daiichi Sankyo <i>Parsippany, NJ</i>	acute ischemic stroke	Phase I/II www.dsi.com
EG-1962 (nimodipine microparticles) ORPHAN DRUG	Edge Therapeutics <i>Berkeley Heights, NJ</i>	prevention of cerebral ischemia following aneurysmal subarachnoid hemorrhage	Phase I/II www.edgetherapeutics.com
GM6 (peptide therapeutic)	Genervon Biopharmaceuticals <i>Pasadena, CA</i>	acute ischemic stroke	Phase II www.genervon.com
MP-124 (PARP inhibitor)	Mitsubishi Tanabe Pharma <i>Jersey City, NJ</i>	acute ischemic stroke	Phase I www.mt-pharma-america.com
MultiStem® allogeneic stem cell therapy	Athersys <i>Cleveland, OH</i>	ischemic stroke <i>(see also heart attack)</i>	Phase II www.athersys.com
NA-1 (PDZ domain inhibitor)	Arbor Vita <i>Sunnyvale, CA</i> NoNO <i>Toronto, Canada</i>	stroke	Phase II www.nonoinc.com

Stroke

<u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
NSI-566 (spinal cord-derived neural stem cell therapy)	Neuralstem <i>Germantown, MD</i>	ischemic stroke	Phase II www.neuralstem.com
PF-05230907	Pfizer <i>New York, NY</i>	intracerebral hemorrhage	Phase I www.pfizer.com
ponezumab (PF-04360365) (beta amyloid inhibitor)	Pfizer <i>New York, NY</i>	cerebral amyloid angiopathy	Phase II www.pfizer.com
Pradaxa [®] dabigatran etexilate	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, NC</i>	secondary stroke prevention following previous embolic stroke, stroke prevention in non-valvular atrial fibrillation	Phase III www.boehringer-ingelheim.com
Sanguinate [™] PEGylated hemoglobin and carbon monoxide	Prolong Pharmaceuticals <i>South Plainfield, NJ</i>	delayed cerebral ischemia following acute aneurysmal subarachnoid hemorrhage	Phase II www.prolongpharma.com
SB-623 (cell replacement therapy)	Sunovion Pharmaceuticals <i>Marlborough, MA</i>	stroke	Phase II www.sunovion.com
sodium nitrate	Hope Pharmaceuticals <i>Scottsdale, AZ</i>	reversal of cerebral vasospasm after subarachnoid hemorrhage (<i>see also heart attack</i>)	Phase II www.hopepharm.com
Stemedyne [™] -MSC mesenchymal stem cell therapy	Semedica Cell Technologies <i>San Diego, CA</i>	ischemic stroke (<i>see also heart attack, heart failure</i>)	Phase II www.stemedica.com
TS01 (urokinase-type plasminogen activator stimulant)	Thrombolytic Science International <i>Cambridge, MA</i>	acute ischemic stroke	Phase I www.tsillc.net

Thrombosis
Product Name

Sponsor

Indication

Development Status

PAR4 antagonist

Bristol-Myers Squibb
Princeton, NJ

thrombosis (antiplatelet)

Phase I
www.bms.com

Savaysa™
edoxaban

Daiichi Sankyo
Parsippany, NJ

venous thrombosis (pediatric)

Phase I
www.dsi.com

tecarfarin
(vitamin K epoxidase inhibitor)

Armetheon
Milpitas, CA

thromboembolism (prevention)

Phase II/III
www.armetheon.com

temanogrel
(serotonin 2A receptor inverse agonist)

Arena Pharmaceuticals
San Diego, CA
Ildong Pharmaceutical
Seoul, South Korea

arterial thrombosis

Phase I
www.arenapharm.com

TS23
(antiplasmin inhibitor)

Daiichi Sankyo
Parsippany, NJ
Thrombolytic Science International
Cambridge, MA

thrombosis

Phase I
www.dsi.com
www.tsillc.net

Xarelto®
rivaroxaban

Bayer HealthCare Pharmaceuticals
Whippany, NJ
Janssen Research & Development
Raritan, NJ

prevention of symptomatic venous thrombo-
embolism and venous thromboembolism-related
death in high-risk, medically ill patients
*(see also acute coronary syndrome, coronary
artery disease, heart failure, peripheral vascular
disease, stroke)*

Phase III
www.pharma.bayer.com
www.janssenrnd.com

Other
Product Name

Sponsor

Indication

Development Status

BVI-007
(thrombopoietin antagonist)

BioVascular
San Diego, CA

lower mortality and secondary cardiovascular events

Phase I
www.biovascularinc.com

CARD-024
(2 alpha hydroxyvitamin D5)

Cardiavent
Ann Arbor, MI

cardiovascular function and health

Phase I completed
www.cardiavent.com

Other <u>Product Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
CardiaPill® aspirin/lisinopril/lovastatin	CardioPharma <i>Wilmington, DE</i>	cardiovascular disorders	in clinical trials www.cardio-pharma.com
clopidogrel nanosomal (intravenous)	Jina Pharmaceuticals <i>Libertyville, IL</i>	cardiovascular disorders	Phase I completed www.jinapharma.com
GoNitro™ nitroglycerin sublingual powder formulation	Espero Pharmaceuticals <i>Jacksonville, FL</i> Pohl Boskamp <i>Hohenlockstedt, Germany</i>	angina pectoris	application submitted www.esperopharma.com
IW-1701 (guanylyl cyclase agonist)	Ironwood Pharmaceuticals <i>Cambridge, MA</i>	cardiovascular disorders	Phase I www.ironwoodpharma.com
IW-1973 (guanylate cyclase agonist)	Ironwood Pharmaceuticals <i>Cambridge, MA</i>	cardiovascular disorders	Phase I www.ironwoodpharma.com
levosimendan (calcium sensitizer)	Tenax Therapeutics <i>Morrisville, NC</i>	reduction of morbidity and mortality in cardiac surgery in patients at risk for low cardiac output syndrome (Fast Track)	Phase III www.tenaxthera.com
Opsumit® macitentan	Actelion Pharmaceuticals <i>South San Francisco, CA</i>	Eisenmenger syndrome (<i>see also pulmonary vascular hypertension</i>)	Phase III www.actelion.com
PA8140 (aspirin 81mg/omeprazole 40mg)	POZEN <i>Chapel Hill, NC</i>	secondary prevention of cardiovascular and cerebrovascular disease in patients at risk for aspirin-induced ulcers	application submitted www.pozen.com
PA32540 (aspirin 325mg/omeprazole 40mg)	POZEN <i>Chapel Hill, NC</i>	secondary prevention of cardiovascular and cerebrovascular disease in patients at risk for aspirin-induced ulcers	application submitted www.pozen.com
RX-10001 (inflammation mediator inhibitor)	Resolvyx Pharmaceuticals <i>Cambridge, MA</i>	cardiovascular disorders	Phase I completed www.resolvyx.com

Other Product Name	Sponsor	Indication	Development Status
T-89 (herbal medicine)	Tasly Pharmaceuticals <i>Rockville, MD</i>	angina pectoris	Phase III www.taslyus.com
udenafil ORPHAN DRUG	Mezzion Pharma <i>Seoul, South Korea</i>	congenital heart defect (single functional ventricle)	Phase I/II completed www.mezzion.co.kr

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 November 6, 2015.** The medicines in this listing 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 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 website, at www.phrma.org.

Definitions

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

Fast Track—Upon request by a sponsor, the FDA can grant this designation to facilitate the development and expedite the review of a drug or biologic to treat a serious condition and fill an unmet medical need. When considering a biopharmaceutical company’s request for Fast Track designation for an investigational drug or biologic, the FDA evaluates whether it will affect factors such as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one, and whether a condition can be adequately addressed by available therapy. With Fast Track designation, early and frequent communication between the FDA and the biopharmaceutical company is encouraged throughout the entire drug development and review process to help to quickly resolve any questions or issues that arise, potentially leading to an earlier approval and access by patients.

Orphan Designation—Upon request by a sponsor, the FDA can grant special status (“orphan status”) to a drug or biologic to treat a rare disease or condition. In order to receive an orphan designation, a qualifying drug or biologic must be intended for the treatment, diagnosis, or prevention of a rare disease or condition that affects fewer than 200,000 people in the United States, or that affects more than 200,000 persons but is not expected to recover the costs of its development and marketing.

Phase I—Researchers test the investigational drug or biologic 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 investigational drug or biologic is given to volunteer patients, usually between 100 and 500, to determine whether it is effective, identify an optimal dose, and to further evaluate its short-term safety.

Phase III—The investigational drug or biologic is given to a larger, more diverse patient population, often involving between 1,000 and 5,000 patients (but sometimes many more), 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.