

2018 Medicines in Development for Heart Disease and Stroke

Acute Coronary Syndrome

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
CER-001 (recombinant HDL)	Cerenis Therapeutics Labège, France	reduce risk of cardiovascular events post-acute coronary syndrome	Phase II www.cerenis.com
dalcetrapib (CETP inhibitor)	DalCor Pharmaceuticals San Mateo, CA	acute coronary syndrome (genetically-defined population)	Phase III www.dalcorpharma.com
Praluent® alirocumab	Regeneron Tarrytown, NY Sanofi Bridgewater, NJ	acute coronary syndrome (see also lipid disorders)	Phase III www.regeneron.com www.sanofi.com

Adjunctive Therapies

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
andexanet alfa ORPHAN DRUG	Portola Pharmaceuticals South San Francisco, CA	anticoagulant reversal (Fxa inhibitor)	application submitted www.portola.com
ciraparantag	Perosphere Danbury, CT	anticoagulant reversal (Fast Track)	Phase II www.perospherepharma.com
CMX-2043 (proto-oncogene-protein-c-akt modulator)	Ischemix North Grafton, MA	reduce cardiac injury in patients undergoing percutaneous coronary intervention (PCI)	Phase II completed www.ischemix.com

Adjunctive Therapies

Drug Name

Sponsor

Indication

Development Status

Kengreal®
cangrelor

Chiesi USA
Cary, NC

partial or complete obstruction of systemic to pulmonary artery shunt in patients at risk for thrombosis (neonates)

Phase I
www.chiesiusa.com

levosimendan IV
(R-enantiomer of simendan)
ORPHAN DRUG

Tenax Therapeutics
Morrisville, NC

low cardiac output syndrome prevention in high risk cardiac surgery (see also pulmonary vascular disease)

Phase III
www.tenaxthera.com

Arrhythmias

Drug Name

Sponsor

Indication

Development Status

bucindolol
(beta blocker/vasodilator)

ARCA Biopharma
Westminster, CO

prevention of symptomatic atrial fibrillation/atrial flutter in patients with heart failure (Fast Track)

Phase II/III
www.arcabio.com

budiodarone
(calcium, potassium, sodium channel antagonist)

Espero Biopharma
Jacksonville, FL

atrial fibrillation, ventricular tachycardia in patients with implantable cardioverter defibrillators

Phase II
www.esperobio.com

etripamil
(calcium channel antagonist)

Milestone Pharmaceuticals
Quebec, Canada

treatment of symptomatic acute episodes of paroxysmal supraventricular tachycardia

Phase II
www.milestonepharma.com

flecainide inhalation
(sodium channel antagonist)

InCarda Therapeutics
Brisbane, CA

paroxysmal atrial fibrillation

Phase I
www.ioncardatherapeutics.com

Arrhythmias

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
vernakalant IV ORPHAN DRUG	Cardiome Pharma Vancouver, Canada	atrial fibrillation	Phase III completed www.cardiome.com

Cardiomyopathy

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
ARRY-797 (p38 mitogen-activated protein kinase inhibitor)	Array BioPharma Boulder, CO	LMNA-related dilated cardiomyopathy	Phase II www.arraybiopharma.com
CAP-1002 (allogeneic cardiosphere-derived stem cell therapy)	Capricor Therapeutics Beverly Hills, CA	Duchenne muscular dystrophy-related cardiomyopathy (see also heart attack)	Phase I/II www.capricor.com
MYK-461/SAR439152 (myosin inhibitor) ORPHAN DRUG	MyoKardia South San Francisco, CA Sanofi Bridgewater, NJ	symptomatic, obstructive hypertrophic cardiomyopathy	Phase II www.myokardia.com
		non-obstructive hypertrophic cardiomyopathy	Phase I www.myokardia.com
MYK-491 (allosteric activator of myosin)	MyoKardia South San Francisco, CA Sanofi Bridgewater, NJ	dilated cardiomyopathy	Phase I www.myokardia.com

Cardiomyopathy

Drug Name

Sponsor

Indication

Development Status

PB-1046
(VPAC2 selective agonist)
ORPHAN DRUG

PhaseBio Pharmaceuticals
Malvern, PA

Duchenne muscular dystrophy-
induced cardiomyopathy
(see also heart failure, pulmonary
vascular disease)

Phase I
www.phasebio.com

tafamidis meglumine
(amyloid inhibitor)
ORPHAN DRUG

Pfizer
New York, NY

transthyretin amyloid cardiomyopathy
(Fast Track)

Phase III
www.pfizer.com

Coronary Artery Disease

Drug Name

Sponsor

Indication

Development Status

apabetalone
(BET protein inhibitor)

Resverlogix
San Francisco, CA

secondary prevention of major
adverse cardiac events (MACE) in
patients with coronary artery disease,
type 2 diabetes and low HDL
cholesterol

Phase III
www.resverlogix.com

AZD5718
(5-lipoxygenase activating
protein inhibitor)

AstraZeneca
Wilmington, DE

coronary artery disease

Phase II
www.astrazeneca.com

Brilinta®
ticagrelor

AstraZeneca
Wilmington, DE

cardiovascular outcomes in patients
with coronary artery disease and
type 2 diabetes without a previous
history of myocardial infarction
or stroke

Phase III
www.astrazeneca.com

Coronary Artery Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
COMBO Stent™ (anti-CD34 mAb/sirolimus drug eluting stent)	OrbusNeich Fort Lauderdale, FL	prevention of coronary artery restenosis in patients with coronary artery disease	in clinical trials www.orbusneich.com
CVBT-141H (fibroblast growth factor-1)	CardioVascular BioTherapeutics Dallas, TX	severe coronary heart disease	Phase II www.cvbt.com
DP9 (progesterone transdermal)	Dimera Portland, OR	myocardial ischemia	Phase II completed www.dimera.net
Generx alferminogene tadenovec (recombinant angiogenic gene therapy)	Angionetics San Diego, CA	refractory angina due to myocardial ischemia (cardiac microvascular insufficiency) (Fast Track)	Phase III www.angionetics.com
MEDI5884 (cholesterol modulator)	MedImmune Gaithersburg, MD	coronary heart disease	Phase II www.medimmune.com
MEDI6012 (LCAT therapy)	MedImmune Gaithersburg, MD	coronary artery disease	Phase II www.medimmune.com
ridaforolimus eluting coronary stent (device drug combination)	Medinol Tel Aviv, Israel	coronary artery restenosis	Phase III www.medinol.com
umirolimus (drug-eluting stent)	Biosensors International Singapore	coronary artery restenosis	Phase III www.biosensors.com

Coronary Artery Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
VB-201	VBL Therapeutics Modi'in, Israel	atherosclerosis	Phase II www.vblrx.com

Heart Attack

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
BVI-007 (thrombopoietin inhibitor)	BioVascular San Diego, CA	prevention of myocardial infarction in patients who have had a previous cardiovascular event (see also stroke)	Phase I www.biovascularinc.com
CAP-1002 (allogeneic cardiosphere-derived stem cell therapy)	Capricor Therapeutics Beverly Hills, CA	myocardial infarction (see also cardiomyopathy)	Phase I/II www.capricor.com
CSL 112 (apolipoprotein A-I infusion therapy)	CSL Behring King of Prussia	reduction of recurrent cardiovascular events following myocardial infarction	Phase II www.cslobehring.com
Entresto [®] sacubitril/valsartan	Novartis East Hanover, NJ	post-acute myocardial infarction (see also heart failure)	Phase III www.novartis.com
FDY-5301	Faraday Pharmaceuticals Seattle, WA	myocardial infarction	Phase II www.faradaypharma.com

Heart Attack

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
mesenchymal stem cell therapy (ischemic-tolerant stem cells)	Stemmedica Cell Technologies San Diego, CA	acute myocardial infarction (see also heart failure, stroke)	Phase I completed www.stemedica.com
MultiStem® allogeneic stem cell therapy	Athersys Cleveland, OH	acute myocardial infarction (see also stroke)	Phase II www.athersys.com
REC-01 (CD26 antigen inhibitor)	Recardio San Francisco, CA	acute myocardial infarction	Phase I www.recardio.eu
RGN-352 injectable (thymosin beta-4)	RegeneRx Biopharmaceuticals Rockville, MD	acute myocardial infarction (see also stroke)	Phase I completed www.regenerx.com
TF0023 (aspirin pro-drug)	Techfields Pharma Dover, DE	heart attack recovery (see also stroke)	Phase II www.tfpharma.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
AdipoCell™ adipose-derived autologous stem cell therapy	U.S. Stem Cell Miami, FL	congestive heart failure	Phase I/II www.us-stemcell.com
Aironite sodium nitrite inhalation	Savara Pharmaceuticals Austin, TX	diastolic heart failure	Phase II www.savarapharma.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
AMG 986 (apelin receptor agonist)	Amgen Thousand Oaks, CA	heart failure	Phase I www.amgen.com
AR-06 (hydralazine/isosorbide dinitrate controlled release)	Arbor Pharmaceuticals Atlanta, GA	heart failure	Phase III www.arborpharma.com
AZD4831 (myeloperoxidase modulator)	AstraZeneca Wilmington, DE	heart failure with a preserved ejection fraction	Phase I www.astrazeneca.com
BAY1142524 (chymase inhibitor)	Bayer HealthCare Pharmaceuticals Whippany, NJ	left ventricular dysfunction (heart failure)	Phase II www.pharma.bayer.com
BMS-986224	Bristol-Myers Squibb Princeton, NJ	chronic heart failure	Phase I www.bms.com
BMS-986231 (nitroxyl donor)	Bristol-Myers Squibb Princeton, NJ	acute heart failure	Phase II www.bms.com
BR6819 (vasopressin receptor antagonist)	Bayer HealthCare Pharmaceuticals Whippany, NJ	heart failure	Phase I www.pharma.bayer.com
CardiALLO™ (allogenic culture expanded mesenchymal stem cells derived from bone marrow)	BioCardia San Carlos, CA	heart failure	Phase I www.biocardia.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
CLR325	Novartis East Hanover, NJ	chronic stable heart failure	Phase II www.novartis.com
elamipretide	Stealth BioTherapeutics Newton, MA	acute heart failure, heart failure with preserved ejection fraction, heart failure with reduced ejection fraction	Phase II www.stealthbt.com
Entresto [®] sacubitril/valsartan	Novartis East Hanover, NJ	heart failure with preserved ejection fraction (see also heart attack)	Phase III www.novartis.com
EZR104 (valsartan extended release)	Ezra Pharma Little Rock, AK	heart failure (see also hypertension)	application submitted www.ezrapharma.com
Farxiga [®] dapagliflozin	AstraZeneca Wilmington, DE	worsening heart failure or cardiovascular death in patients with chronic heart failure (see also other)	Phase III www.astrazeneca.com
Furoscix subcutaneous furosemide	scPharmaceuticals Burlington, MA	chronic heart failure	application submitted www.scpharmaceuticals.com
		decompensated heart failure	Phase II/III www.scpharmaceuticals.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
GSK2798745 (TRPV4 antagonist)	GlaxoSmithKline Research Triangle Park, NC	heart failure	Phase II www.gsk.com
Injectafer® ferric carboxymaltose	Daiichi Sankyo Basking Ridge, NJ Luitpold Pharmaceuticals Shirley, NY	heart failure with iron deficiency and with a reduced ejection fraction	Phase III www.dsi.com
IW-1973 (soluble guanylate cyclase agonist)	Ironwood Pharmaceuticals Cambridge, MA	heart failure with preserved ejection fraction	Phase II www.ironwoodpharma.com
ixmyelocel-T (stem cell therapy) ORPHAN DRUG	Vericel Cambridge, MA	heart failure due to ischemic dilated cardiomyopathy (Fast Track)	Phase II completed www.vcel.com
Jardiance® empagliflozin	Boehringer Ingelheim Ridgefield, CT Eli Lilly Indianapolis, IN	heart failure with preserved ejection fraction	Phase III www.boehringer-ingelheim.com
JVS-100 (non-viral gene therapy expressing SDF-1)	Juventas Therapeutics Cleveland, OH	heart failure (Fast Track) (see also peripheral vascular disease)	Phase II www.juventasinc.com
LIK066 (SGLT 1/2 inhibitor)	Novartis East Hanover, NJ	patients with type 2 diabetes and heart failure	Phase II www.novartis.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
long-acting loop diuretic	Sarfez Pharmaceuticals Vienna, VA	chronic congestive heart failure	Phase II www.sarfezpharma.com
mesenchymal stem cell therapy (ischemic-tolerant stem cells)	Stemedica Cell Technologies San Diego, CA	chronic heart failure (see also heart attack, stroke)	Phase II www.stemedica.com
MPC-150-IM (human mesenchymal stem cell therapy)	Mesoblast New York, NY	advanced heart failure	Phase III www.mesoblast.com
		end-stage heart failure	Phase II www.mesoblast.com
MyoCell [®] muscle-derived autologous stem cell therapy	U.S. Stem Cell Sunrise, FL	severe heart damage in heart failure	Phase II/III www.us-stemcell.com
neladenoson bialanate (adenosine A1 receptor agonist)	Bayer HealthCare Pharmaceuticals Whippany, NJ	chronic heart failure	Phase II www.pharma.bayer.com
Neucardin recombinant human neuregulin-1 beta	Zensun USA San Diego, CA	chronic heart failure	Phase II www.zensunus.com
omecamtiv mecarbil (cardiac myosin activator)	Cytokinetics South San Francisco, CA Amgen Thousand Oaks, CA	heart failure	Phase III www.amgen.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Opsumit® macitentan	Actelion Pharmaceuticals South San Francisco, CA	heart failure with preserved ejection fraction and pulmonary arterial disease (see also pulmonary vascular disease, other)	Phase II www.actelion.com
PB-1046 (VPAC2 selective agonist)	PhaseBio Pharmaceuticals Malvern, PA	heart failure with preserved or reduced ejection fraction (see also cardiomyopathy, pulmonary vascular disease)	Phase II www.phasebio.com
PL-3994 NPR-A (cyclic natriuretic peptide receptor A agonist)	Palatin Technologies Cranbury, NJ	heart failure	Phase II www.palatin.com
REC-02 (chemokine CXCL12 modulator)	Recardio San Francisco, CA	congestive heart failure	Phase I www.recardio.eu
RT-100 (gene therapy)	Renova Therapeutics San Diego, CA	congestive heart failure (Fast Track)	Phase III www.renovatherapeutics.com
RT-400 (peptide therapy)	Renova Therapeutics San Diego, CA	acute decompensated heart failure	Phase II www.renovatherapeutics.com
SAR440181 (DCM1 myosin activation)	Sanofi Bridgewater, NJ	post acute heart failure	Phase I www.sanofi.com

Heart Failure

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
SERCA 2a gene therapy	Theragene Pharmaceuticals San Diego, CA	NYHA class III/IV heart failure (Fast Track)	Phase II www.theragenepharma.com
TD-0714 (neprilysin inhibitor)	Theravance Biopharma South San Francisco, CA	heart failure	Phase I www.theravance.com
TD-1439 (neprilysin inhibitor)	Theravance Biopharma South San Francisco, CA	heart failure	Phase I www.theravance.com
ularitide (atrial peptide agonist/diuretic)	Cardiorentis Zug, Switzerland	acute heart failure (Fast Track)	Phase III www.cardiorentis.com
vericiguat (sGC stimulator)	Bayer HealthCare Pharmaceuticals Whippany, NJ	chronic heart failure	Phase III www.pharma.bayer.com

Hypertension

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
AF-130 (purinergic P2X3 receptor antagonist)	Merck Kenilworth, NJ	hypertension	Phase I completed www.merck.com
aprocitanan (dual endothelin receptor antagonist)	Idorsia Pharmaceuticals Allschwil, Switzerland Janssen Biotech Horsham, PA	resistant hypertension management	Phase II www.adorsia.com www.janssen.com

Hypertension

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
atorvastatin/aspirin/ramipril fixed-dose combination (polypill)	Ferrer Internacional Barcelona, Spain	hypertension	Phase II www.ferrer.com
B244 (bacteria-based therapeutic)	AOBiome Cambridge, MA	hypertension	Phase II www.aobiome.com
digoxin immune Fab ORPHAN DRUG	AMAG Pharmaceuticals Waltham, MA	severe preeclampsia (Fast Track)	Phase II/III www.amagpharma.com
Edarbi® azilsartan medoxomil	Arbor Pharmaceuticals Atlanta, GA	hypertension (pediatric)	Phase III www.arborpharma.com
EZR104 (valsartan extended release)	Ezra Pharma Little Rock, AK	hypertension (see also heart failure)	application submitted www.ezrapharma.com
IONIS-AGT-LRX (LICA-conjugated antisense drug)	Ionis Pharmaceuticals Carlsbad, CA	treatment resistant hypertension	Phase II www.ionispharma.com
KBP-5074 (mineralocorticoid receptor antagonist)	KBP Biosciences Princeton, NJ	hypertension in advanced chronic kidney disease	Phase I/II www.kbpbiosciences.com
KIT-302 (amlodipine/celecoxib fixed-dose combination)	Kitov Pharmaceuticals Tel Aviv, Israel	treatment of hypertension and osteoarthritis pain simultaneously	application submitted www.kitovpharma.com

Hypertension

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Kybiqo olmesartan medoxomil/rosuvastatin fixed-dose combination	Stocasil Industry, CA	hypertension and hyperlipidemia (see also lipid disorders)	Phase II www.stocosil.com
LHW090	Novartis East Hanover, NJ	resistant hypertension	Phase II www.novartis.com
QGC001 (brain aminopeptidase A inhibitor)	Quantum Genomics Paris, France	hypertension	Phase II www.quantum-genomics.com
RMJH-111b (magnesium citrate)	RMJ Holdings Ashburn, VA	essential hypertension	Phase I/II completed

Lipid Disorders

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
1-MNA (active metabolite of niacin)	Cortria Boston, MA Pharmena Lodz, Poland	hyperlipidemia	Phase II completed www.pharmena.eu
AKCEA-ANGPTL3-LRX (ANGPTL3 protein inhibitor)	Akcea Therapeutics Cambridge, MA	rare hyperlipidemias	Phase II www.akceatx.com
AKCEA-APO(a)-LRX (ligand conjugated antisense drug)	Akcea Therapeutics Cambridge, MA	hyperlipoproteinemia with significant cardiovascular risk	Phase II www.akceatx.com

Lipid Disorders

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
AKCEA-APOCIII-LRX (ligand conjugated antisense drug)	Akcea Therapeutics Cambridge, MA	hypertriglyceridemia	Phase II www.akceatx.com
AMG 899 (CETP inhibitor)	Amgen Thousand Oaks, CA	dyslipidemia	Phase II www.amgen.com
ARI-3037MO (GPR109A/GPR109B receptor agonist)	Arisaph Pharmaceuticals Boston, MA	dyslipidemia, hypertriglyceridemia	Phase II www.arisaph.com
bempedoic acid (oral)	Esperion Therapeutics Ann Arbor, MI	lowering elevated low-density lipoprotein (LDL) cholesterol, cardiovascular disease risk reduction	Phase III www.esperion.com
bempedoic acid/ezetimibe fixed-dose combination (oral)	Esperion Therapeutics Ann Arbor, MI	lowering elevated LDL cholesterol	Phase III www.esperion.com
CaPre® long-chain Omega-3 phospholipid	Acasti Pharma Quebec, Canada	hypertriglyceridemia	Phase II completed www.ascatipharma.com
Epanova® omega-3 carboxylic acids	AstraZeneca Wilmington, DE	high-risk for cardiovascular events in patients with persistent hypertriglyceridemia and low HDL cholesterol	Phase III www.astrazeneca.com
evinacumab (REGN1500) (ANGPTL-1 antibody)	Regeneron Tarrytown, NY	homozygous familial hypercholesterolemia	Phase II www.regeneron.com

Lipid Disorders

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
gemcabene (acetyl-CoA carboxylase inhibitor/ lipoprotein A inhibitor) ORPHAN DRUG	Gemphire Therapeutics Livonia, MI	severe hypertriglyceridemia, homozygous familial hypercholesterolemia, heterozygous familial hypercholesterolemia	Phase II www.gemphire.com
inclisiran (RNAi therapeutic)	The Medicines Company Parsippany, NJ	hypercholesterolemia	Phase III www.themedicinescompany.com
K-312	Kowa Research Institute Morrisville, NC	dyslipidemia	Phase I www.kowaus.com
Kybiqo olmesartan medoxomil/rosuvastatin fixed-dose combination	Stocasil Industry, CA	hypertension and hyperlipidemia (see also hypertension)	Phase II www.stocasil.com
Kynamro® mipomersen	Kastle Therapeutics Chicago, IL	heterozygous familial hypercholesterolemia	Phase II completed www.kastletherapeutics.com
MGL-3196 (liver-directed thyroid hormone receptor beta agonist)	Madrigal Pharmaceuticals West Conshohocken, PA	heterozygous familial hypercholesterolemia	Phase II www.madrigalpharma.com
pemafibrate (K-877) (selective PPAR-alpha modulator)	Kowa Research Institute Morrisville, NC	dyslipidemia	Phase III www.kowaus.com
PF-06427878 (DGAT2 inhibitor)	Pfizer New York, NY	hyperlipidemia	Phase I www.pfizer.com

Lipid Disorders

Drug Name

Sponsor

Indication

Development Status

Praluent®
alirocumab
ORPHAN DRUG

Regeneron
Tarrytown, NY
Sanofi
Bridgewater, NJ

homozygous familial
hypercholesterolemia
(see also acute coronary syndrome)

Phase III
www.regeneron.com
www.sanofi.com

RGX 501
(personalized gene therapy)
ORPHAN DRUG

REGENXBIO
Rockville, MD
University of Pennsylvania
Philadelphia, PA

homozygous familial
hypercholesterolemia

Phase I/II
www.regenxbio.com

saroglitazar

Zydus Cadila
Gujarat, India

dyslipidemia (≥ 500 mg/dL)

Phase II
www.zyduscadila.com

SC401
(docosahexaenoic acid/
eicosapentaenoic acid)

Sancilio
Riveria Beach, FL

severe hypertriglyceridemia

Phase II
www.sancilio.com

VK-2809
(thyroid hormone receptor
beta agonist)

Viking Therapeutics
San Diego, CA

hypercholesterolemia

Phase II
www.vikingtherapeutics.com

volanesoren
(antisense ApoCIII inhibitor)
ORPHAN DRUG

Akcea Therapeutics
Cambridge, MA

familial chylomicronemia
syndrome

application submitted
www.akceatx.com

Peripheral Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
ACP-01 (angiogenic cell precursor therapy)	Hemostemix Calgary, Canada	critical limb ischemia	Phase II www.hemostemix.com
ALD-301 (bone marrow-derived adult stem cells)	Aldagen Durham, NC	peripheral arterial occlusive disorders	Phase II completed
ASCT01 (autologous stem cell therapy)	Lifecells Irvine, CA	critical limb ischemia	Phase I/II www.lifecellslc.com
autologous stem cell therapy	BioTech Holdings Richmond, CA	ischemia associated with diabetes	in clinical trials
BAY1193397 (AR alpha-2c receptor antagonist)	Bayer HealthCare Pharmaceuticals Whippany, NJ	peripheral arterial disease	Phase II www.pharma.bayer.com
bepermingene perplasmid (HGF plasmid)	AnGes USA Bethesda, MD Mitsubishi Tanabe Pharma Osaka, Japan	critical limb ischemia (Fast Track)	Phase III www.anges.co.jp
CVBT-141C (fibroblast growth factor-1)	CardioVascular BioTherapeutics Dallas, TX	peripheral artery disease	Phase II www.cvbt.com
human plasma-derived fibrinolysin ORPHAN DRUG	Grifols Therapeutics Los Angeles, CA	acute peripheral arterial occlusion	Phase II www.grifols.com

Peripheral Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
JVS-100 (non-viral gene therapy)	Juventas Therapeutics Cleveland, OH	peripheral artery disease (Fast Track) (see heart failure)	Phase II www.juventasinc.com
Liprostin™ alprostadil (liposomal controlled release)	AngioSoma Montgomery, TX	peripheral artery disease	Phase II www.antisomainfo
LLG783 (LDL receptor antagonist mAb)	Novartis East Hanover, NJ	intermittent claudication, peripheral arterial disorder	Phase II www.novartis.com
MABp1 (IL-1-alpha/IgG1 mAb)	XBiotech Austin, TX	peripheral vascular disease (Fast Track)	Phase II www.xbiotech.com
MultiGeneAngio peripheral arterial disease cell therapy	MultiGene Vascular Systems Haifa, Israel	peripheral arterial disease	Phase I/II www.mgvs.co.il
NVS therapy (peripheral vascular disorder drug-device therapy)	Alucent Medical Salt Lake City, UT	peripheral vascular disease	Phase I www.alucentmedical.com
PLX-PAD cell therapy	Pluristem Therapeutics Haifa, Israel	critical limb ischemia (Fast Track)	Phase III www.pluristem.com
SB-030 (inflammation mediator modulator)	Symic Bio Emeryville, CA	peripheral arterial disease	Phase II www.symic.bio

Peripheral Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
TV1001SR (sodium nitrate oral)	Theravasc Cleveland, OH	peripheral arterial disease	Phase II www.theravasc.com
VM202 (donaperminogene seltoplasmid)	ViroMed Seoul, South Korea	peripheral artery disease	Phase III www.viomed.co.kr
vonapanitase (recombinant human elastase) ORPHAN DRUG	Proteon Therapeutics Waltham, MA	peripheral artery disease (Fast Track)	Phase III www.proteontherapeutics.com
Xarelto® rivaroxaban	Bayer HealthCare Pharmaceuticals Whippany, NJ Janssen Raritan, NJ	infrainguinal peripheral arterial disease (see also stroke, thrombosis, other)	Phase III www.pharma.bayer.com www.janssen.com

Pulmonary Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
ABI-009 (sirolimus albumin bound nanoparticle)	Aadi Pacific Palisades, CA	pulmonary arterial hypertension	Phase I
ambrisentan/tadalafil fixed-dose combination	GlaxoSmithKline Research Triangle Park, NC	pulmonary arterial hypertension	Phase I completed www.gsk.com

Pulmonary Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
bardoxolone methyl (Nrf2 activator) ORPHAN DRUG	Reata Pharmaceuticals Irving, TX	connective tissue disease associated with pulmonary arterial hypertension (CTD-PAD)	Phase III www.reatapharma.com
		pulmonary hypertension-interstitial lung disease (PH-ILD)	Phase II www.reatapharma.com
beraprost 314d	Lung Biotechnology Silver Spring, MD	pulmonary arterial hypertension	Phase III www.lungbiotechnology.com
CAM2043 (treprostinil controlled release)	Camurus Lund, Sweden	pulmonary arterial hypertension	Phase I/II www.camurus.com
GeNOsyl nitric oxide inhalation	GeNO Atlanta, GA	pulmonary arterial hypertension	Phase II completed www.genollic.com
GSK2256098 (FAK inhibitor)	GlaxoSmithKline Research Triangle Park, NC	pulmonary arterial hypertension	Phase I completed www.gsk.com
GSK2586881 (recombinant human angiotensin converting enzyme)	GlaxoSmithKline Research Triangle Park, NC	pulmonary arterial hypertension	Phase I completed www.gsk.com
INOpulse nitric oxide inhalation ORPHAN DRUG	Bellerophon Therapeutics Warren, NJ	pulmonary arterial hypertension	Phase III www.bellerophon.com

Pulmonary Vascular Disease

Drug Name

Sponsor

Indication

Development Status

INS1009
(inhaled, sustained-release
nebulized prodrug formulation
of treprostinil)

Insmed
Bridgewater, NJ

pulmonary arterial hypertension

Phase I
www.insmed.com

KAR5585
(tryptophan hydroxylase 1 inhibitor)
ORPHAN DRUG

Karos Pharmaceuticals
New Haven, CT

pulmonary arterial hypertension

Phase I

Letairis®
ambrisentan

Gilead Sciences
Foster City, CA
GlaxoSmithKline
Research Triangle Park, NC

pulmonary arterial hypertension
(pediatric)

Phase II
www.gilead.com
www.gsk.com

levosimendan IV
(R-enantiomer of simendan)

Tenax Therapeutics
Morrisville, NC

pulmonary hypertension due to heart
failure with preserved ejection fraction
(see also adjunctive therapies)

Phase II
www.tenaxthera.com

LIQ861
(inhalation)

Liquidia Technologies
Morrisville, NC

pulmonary arterial hypertension

Phase III
www.liquidia.com

Opsumit®
macitentan
ORPHAN DRUG

Actelion Pharmaceuticals
South San Francisco, CA

pulmonary arterial hypertension
(pediatric), portopulmonary
hypertension
(see also heart failure, other)

Phase III
www.actelion.com

chronic thromboembolic pulmonary
hypertension

Phase II
www.actelion.com

Pulmonary Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
OreniLeft™ treprostinil	United Therapeutics Silver Spring, MD	pulmonary arterial hypertension associated with left ventricular diastolic dysfunction (WHO group 2)	Phase III www.unither.com
PB-1046 (VPAC2 selective agonist) ORPHAN DRUG	PhaseBio Pharmaceuticals Malvern, PA	pulmonary arterial hypertension (see also cardiomyopathy, heart failure)	Phase II www.phasebio.com
ralinepag (prostacyclin receptor agonist) ORPHAN DRUG	Arena Pharmaceuticals San Diego, CA	pulmonary arterial hypertension	Phase II www.arenapharm.com
RemoSynch™ implantable system for Remodulin® (treprostinil)	United Therapeutics Silver Spring, MD	pulmonary arterial hypertension	application submitted www.unither.com
RemUnity™ treprostinil continuous subcutaneous via pre-filled pump	United Therapeutics Silver Spring, MD	pulmonary arterial hypertension	Phase III www.unither.com
sGC activator 2 (soluble guanylate cyclase)	Bayer HealthCare Pharmaceuticals Whippany, NJ	pulmonary hypertension	Phase I www.pharma.bayer.com
sildenafil	Pfizer New York, NY	persistent pulmonary arterial hypertension (neonates)	Phase III www.pfizer.com

Pulmonary Vascular Disease

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
tacrolimus ORPHAN DRUG	VIVUS Campbell, CA	pulmonary arterial hypertension	Phase II www.vivus.com
Trevyent treprostinil patch pump ORPHAN DRUG	SteadyMed Therapeutics San Ramon, CA	pulmonary arterial hypertension	application submitted www.steadymed.com
Tysuberprost™ esuberaprost in combination with Tyvaso® (treprostinil)	United Therapeutics Silver Spring, MD	pulmonary arterial hypertension (decrease morbidity and mortality)	Phase III www.unither.com
Tyvaso® treprostinil	United Therapeutics Silver Spring, MD	pulmonary arterial hypertension associated with chronic obstructive pulmonary disease (WHO group 3)	Phase III www.unither.com
Tyvaso-ILD™ treprostinil	United Therapeutics Silver Spring, MD	pulmonary arterial hypertension associated with idiopathic pulmonary fibrosis (WHO group 3)	Phase III www.unither.com
Uptravi® selexipag intravenous	Actelion Pharmaceuticals South San Francisco, CA	pulmonary arterial hypertension (switch from oral to intravenous)	Phase III www.actelion.com
VentaProst epoprostenol inhalation	Aerogen Pharma Galway, Ireland	pulmonary hypertension	Phase II www.aerogen.com

Stroke

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
3K3A-APC (recombinant human wild-type activated protein C)	ZZ Biotech Houston, TX	moderate to severe ischemic stroke	Phase II www.zzbiotech.com
BIB093 (glibenclamide IV) ORPHAN DRUG	Biogen Cambridge, MA	large hemispheric infarction (severe form of ischemic stroke) (Fast Track)	Phase II www.biogen.com
BVI-007 (thrombopoietin inhibitor)	BioVascular San Diego, CA	prevention of thrombotic stroke in patients who have had a previous cardiovascular event (see also heart attack)	Phase I www.biovascularinc.com
clazosentan (endothelin receptor antagonist) ORPHAN DRUG	Idorsia Pharmaceuticals Allschwil, Switzerland	cerebral vasospasm associated with aneurysmal subarachnoid hemorrhage	Phase III www.idorsia.com
CN-105 (apolipoprotein E agonist)	AegisCN Raleigh, NC	intracerebral hemorrhage	Phase II
DM199 (recombinant human kallikrein-1)	DiaMedica Therapeutics Minneapolis, MN	acute ischemic stroke	Phase II www.diamedica.com
DS-1040 (TAFI α inhibitor)	Daiichi Sankyo Basking Ridge, NJ	acute ischemic stroke	Phase I www.dsi.com

Stroke

Drug Name

Sponsor

Indication

Development Status

EG-1962
(nimodipine microparticles)
ORPHAN DRUG

Edge Therapeutics
Berkeley Heights, NJ

aneurysmal subarachnoid hemorrhage
(intraventricular delivery) (Fast Track)

Phase III
www.edgetherapeutics.com

aneurysmal subarachnoid hemorrhage
(intracisternal delivery)

Phase I
www.edgetherapeutics.com

LT-3001
(antioxidant/free radical scavenger)

Lumosa Therapeutics
Taipei, Taiwan

acute ischemic stroke

Phase I
www.lumosa.com.tw

MAA868
(anti-FXI mAb)

Novartis
East Hanover, NJ

stroke prevention in atrial fibrillation

Phase II
www.novartis.com

mesenchymal stem cell therapy
(ischemic-tolerant stem cells)

Stemmedica Cell Technologies
San Diego, CA

ischemic stroke
(see also heart attack, heart failure)

Phase II
www.stemedica.com

MultiStem®
allogeneic stem cell therapy

Athersys
Cleveland, OH

ischemic stroke (Fast Track)
(see also heart attack)

Phase II
www.athersys.com

NA-1
(PSD-95 antagonist)

NoNO
Toronto, Canada

stroke with endovascular intervention

Phase III
www.nonoinc.ca

natalizumab
(alpha-4 integrin inhibitor)

Biogen
Cambridge, MA

acute ischemic stroke

Phase II
www.biogen.com

Stroke

Drug Name

Sponsor

Indication

Development Status

NVX-208
(dodecafluoropentane nanoemulsion)

NuvOx Pharma
Tucson, AZ

acute ischemic stroke

Phase I/II
www.nuvoxpharma.com

PF-05230907
(factor Xa protein replacement)
ORPHAN DRUG

Pfizer
New York, NY

intracerebral hemorrhage

Phase I
www.pfizer.com

Pradaxa®
dabigatran etexilate

Boehringer Ingelheim Pharmaceuticals
Ridgefield, CT

secondary stroke prevention in
patients with embolic stroke of
undetermined source
(see also thrombosis)

Phase III
www.boehringer-ingelheim.com

RGN-352 injectable
(thymosin beta-4)

RegeneRx Biopharmaceuticals
Rockville, MD

stroke
(see also heart attack)

Phase I completed
www.regenerx.com

salvinorin A
(opioid kappa receptor agonist)

Neurokappa Therapeutics
Philadelphia, PA

cerebral vasospasm

Phase I

SB623
(modified bone marrow derived
mesenchymal stem cells)

SanBio
Mountain View, CA
Sunovion Pharmaceuticals
Marlborough, MA

ischemic stroke

Phase II
www.sanbio.com
www.sunovion.com

stroke polyfunctional therapeutic

HSRx Biopharmaceutical
Tucson, AZ

stroke

Phase I
www.hsrxbiopharmaceutical.com

Stroke

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
TF0023 (aspirin pro-drug)	Techfields Pharma Dover, DE	ischemic stroke (see also heart attack)	Phase II www.tfpharma.com
Xarelto® rivaroxaban	Bayer HealthCare Pharmaceuticals Whippany, NJ Janssen Raritan, NJ	secondary prevention of stroke in patients who have had an embolic stroke (see also peripheral vascular disease, thrombosis, other)	Phase III www.pharma.bayer.com www.janssen.com

Thrombosis

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
BAY1213790 (anti-FXIIa antibody)	Bayer HealthCare Pharmaceuticals Whippany, NJ	thrombosis	Phase II www.pharma.bayer.com
BAY2306001 (FXI antisense drug/IONIS-FXI)	Bayer HealthCare Pharmaceuticals Whippany, NJ Ionis Pharmaceuticals Carlsbad, CA	thrombosis	Phase II www.pharma.bayer.com
BMS-986177 (fibrinolytic agent)	Bristol-Myers Squibb Princeton, NJ	thrombosis	Phase I www.bms.com

Thrombosis

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Eliquis® apixaban	Bristol-Myers Squibb Princeton, NJ Pfizer New York, NY	acute venous thromboembolism (VTE) (pediatric)	Phase III www.bms.com www.pfizer.com
		thromboembolism (pediatric)	Phase I www.bms.com www.pfizer.com
EP-7041 (factor XIa inhibitor)	eXlithera Pharmaceuticals Westborough, MA	prevention and treatment of thrombosis in patients undergoing surgeries	Phase I www.exithera.com
ichorcumab (recombinant human anti-thrombin antibody)	Janssen Raritan, NJ	thrombosis	Phase I www.janssen.com
isoquercetin (plant flavinoid)	Quercegen Pharmaceutical Sudbury, MA	prevention of thromboembolism in cancer patients	Phase II/III www.quercegen.com
NOV-12	Morphosys Munich, Germany Novartis East Hanover, NJ	prevention of thrombosis	Phase I www.morphosys.com www.novartis.com
Pradaxa® dabigatran etexilate	Boehringer Ingelheim Ridgefield, CT	VTE (pediatric) (see also stroke)	Phase III www.boehringer-ingelheim.com

Thrombosis

Drug Name

Sponsor

Indication

Development Status

tecarfarin

Espero Biopharma
Jacksonville, FL

thrombosis

Phase III
www.esperobio.com

TS23
(alpha-2 plasmin inhibitor
inactivating mAb)

Translational Sciences
Phoenix, AZ

thrombosis

Phase I
www.translationalsciences.com

warfarin breakable tablets

Accu-Break Pharmaceuticals
Plantation, FL

thromboembolism

application submitted

Xarelto®
rivaroxaban

Janssen
Raritan, NJ

prevention of symptomatic VTE and
VTE-related death in high-risk,
medically ill patients
(see also peripheral vascular disease,
stroke, other)

Phase III
www.janssen.com

VTE prevention in high-risk ambulatory
cancer patients

Phase III
www.janssen.com

long-term prevention of recurrent
symptomatic VTE

Phase III
www.janssen.com

Other

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
AMG 529 (asialoglycoprotein receptor 1 inhibitor)	Amgen Thousand Oaks, CA	cardiovascular disorders	Phase I www.amgen.com
AZD8601 (VEGF-A)	AstraZeneca Wilmington, DE	cardiovascular disorders	Phase II www.astrazeneca.com
canakinumab (ACZ885) (anti-IL1 beta mAb)	Novartis East Hanover, NJ	secondary prevention of cardiovascular events	Phase III www.novartis.com
COR-001 (monoclonal antibody)	Corvidia Therapeutics Waltham, MA	cardiovascular disorders	Phase I www.corvidiatx.com
Farxiga [®] dapagliflozin	AstraZeneca Wilmington, DE	renal outcomes and cardiovascular death in patients with chronic kidney disease (see also heart failure)	Phase III www.astrazeneca.com
		cardiovascular outcomes in patients with type 2 diabetes	Phase III www.astrazeneca.com
FP-045 (aldehyde dehydrogenase 2 agonist)	Foresee Pharmaceuticals Newark, DE	cardiovascular disorders	Phase I www.foreseepharma.com

Other

<u>Drug Name</u>	<u>Sponsor</u>	<u>Indication</u>	<u>Development Status</u>
Opsumit® macitentan	Actelion Pharmaceuticals South San Francisco, CA	in patients with congenital heart defects who underwent Fontan-palliation (see also heart failure, pulmonary vascular disease)	Phase III www.actelion.com
SAR247799 (S1P1 agonist)	Sanofi Bridgewater, NJ	cardiovascular disorders	Phase I www.sanofi.com
SAR407899 (rho kinase)	Sanofi Bridgewater, NJ	microvascular angina (Syndrome X)	Phase II www.sanofi.com
SNF472 (hexasodium phytate)	Sanifit San Diego, CA	reduce cardiovascular events in patients undergoing hemodialysis	Phase II www.sanifit.com
sotagliflozin	Sanofi Bridgewater, NJ	reduce cardiovascular events in high risk patients with type 2 diabetes	Phase III www.sanofi.com
T89	Tasly Pharmaceuticals Rockville, MD	chronic stable angina pectoris	Phase III www.taslyus.com
TD-9855 (monoamine reuptake inhibitor)	Theravance Biopharma South San Francisco, CA	orthostatic hypotension	Phase I www.theravance.com
udenafil (type 5 cyclic nucleotide phosphodiesterase inhibitor)	Mezzion Pharma Seoul, South Korea	single ventricle congenital heart disease (adolescents)	Phase III www.mezzion.co.kr

Other

Drug Name

Sponsor

Indication

Development Status

Xarelto®
rivaroxaban

Bayer HealthCare Pharmaceuticals
Whippany, NJ
Janssen
Raritan, NJ

reduce risk of MACE in patients with
coronary artery disease or peripheral
artery disease
(see also peripheral vascular disease,
stroke, thrombosis)

application submitted
www.pharma.bayer.com
www.janssen.com

reduce risk of MACE in patients with
congestive heart failure and significant
coronary artery disease

Phase III
www.pharma.bayer.com
www.janssen.com

The content of this report has been obtained through public, government and industry sources, and the Springer "Adis Insight" database based on the latest information. Report current **as of January 24, 2018**. The medicines in this listing include medicines being developed by U.S.-based companies conducting trials in the United States abroad, PhRMA-member companies conducting trials in the United States and abroad, and foreign companies conducting clinical trials in the United States. Some products may not be in active clinical trials. 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: 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 usually fewer than 200,000 people in the United States.

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.