



Cardiovascular - Circulatory System

The cardiovascular system (also known as the circulatory system) is composed of the heart, blood, and blood vessels. The system is known as a closed system because the blood never leaves the system of blood vessels consisting of arteries, capillaries and veins. Arteries deliver oxygenated blood to the tissues and organs whereas veins bring deoxygenated blood back to the heart and lungs. Blood flows from arteries and veins through capillaries, which are the thinnest and most numerous blood vessels.

This is one of the most important systems in the body as none of our cells and tissues can function without adequate oxygen and thus blood supply. If there are any problems with the heart, the rest of the body is greatly affected. Due to our lifestyles, over 50 million Americans have cardiovascular problems, with most other Western countries also facing high and increasing rates. In the United States and European countries, cardiovascular disease is the leading cause of death, usually because it is detected too late and adequate therapeutic measures can no longer be taken. Health can be improved through healthy eating, exercise, and not smoking.

Acute Coronary Syndrome

Acute coronary syndrome (ACS) is chest pain of cardiac origin, often associated with an abnormal electrocardiogram (ECG). It is the most common indicator of heart attack and is largely synonymous with unstable angina. The pain may occur suddenly, often while at rest, worsens, and at best only partially responds to nitrate drugs. ACS often reflects damage to the coronaries (arteries) and can be prevented by controlling risk factors related to diet, exercise, smoking, and cholesterol levels. Hypertension and diabetes should be controlled if these are present in the patient. Aspirin has been shown to reduce the risk of ACS. For more information, refer to the section on myocardial infarction (heart attack).

	COMPANY	PRODUCT	PHASE
Acute Coronary Syndromes	Nuvelo Inc	rNAPc2-injectable	II
	CV Therapeutics, Inc.	Ranexa (ranolazine)	III

Acute Decompensated Heart Failure

Acute decompensated heart failure is when the heart is suddenly unable to pump efficiently. The heart does not stop, but it may operate erratically for a few moments. According to The Annals of Pharmacotherapy, approximately 4.9 million people in the United States were diagnosed with acute decompensated heart failure in 2004. The usual causes are the same as for other heart problems: arterial plaque, stress, smoking, old age, lack of exercise, overwork, and obesity. A family history of the disease exacerbates the problem. Arterial plaque (caused by eating fatty or greasy foods) lines the inside of the arteries that supply the heart with blood. This causes the heart to work extra hard to pump adequate blood throughout the body and causes irregular heartbeats, inefficient blood flow, and a tired heart.

	COMPANY	PRODUCT	PHASE
Acute Decompensated Heart Failure	PDL BioPharma	Ularitide	II

Angina

Angina is chest pain due to lack of blood flow, and hence oxygen, to the heart. This is usually due to the obstruction or spasm of coronary arteries. Coronary artery disease, the main cause of angina, is due to atherosclerosis (hardening of the arteries). Most patients will have a general uncomfortable feeling in their chest, described as a pressure, heaviness, squeezing, burning, or choking sensation. This pain can sometimes be felt in other parts of the body such as the arms and legs. Unstable angina is characterized by sudden onset of angina at rest, and angina lasting for longer than 15 minutes. If these symptoms are experienced, they may signify a heart attack and require urgent medical attention. It is estimated that in the United States, 6.3 million people suffer from angina.

	COMPANY	PRODUCT	PHASE
Angina	Angiogenix, Inc.	Acclaim	II
	CoTherix, Inc.	Fasudil hydrochloride	II
	CV Therapeutics, Inc.	Ranexa (ranolazine)	M

Arrhythmias

Arrhythmias are any of several conditions in which the heart beats either faster or slower than normal. Some arrhythmias are life threatening and can lead to cardiac arrest (the stopping of the heart) and sudden death. Others cause irregular heart beats (palpitations) and can be normal for that particular individual. For adults, the average heart rate ranges from 60 to 100 beats per minute (BPM). The easiest diagnosis is obtained with an electrocardiogram. Treatment often requires heart surgery or installation of a pacemaker. It is estimated that approximately 1 in 8 people or 14.4 million individuals in the United States have some form of arrhythmia.

COMPANY	PRODUCT	PHASE	
CV Therapeutics Inc	Tecadenoson (CVT-510)	III	Arrhythmias
Impax Laboratories Inc	Sotalol Hydrochloride Tablets	M	

Atrial Fibrillation

In atrial fibrillation, a condition affecting 2.3 million Americans, the two upper chambers of the heart (known as the atria) do not beat properly. Blood is not effectively pumped out of the chambers and has a tendency to pool and form a clot. If the clot dislodges and makes its way into the blood stream, it can become caught in a blood vessel in the brain, causing a stroke. Approximately 15 percent of strokes occur in people with atrial fibrillation. Atrial fibrillation is generally related to an underlying heart condition, but is also occasionally attributed to caffeine, alcohol, certain drugs, infections, or other causes.

COMPANY	PRODUCT	PHASE	
ARYx Therapeutics	ATI-2042	II	Atrial Fibrillation
CV Therapeutics Inc	Tecadenoson (CVT-510)	II	
Berlex	Betapace AF (sotalol hydrochloride)	M	

Blood Clot

A blood clot (thrombus) forms due to the aggregation of platelets and clotting factors. These clots form either as a result of injury or a pathologic case of thrombosis. Often, these blood clots form in blood vessels, potentially decreasing or completely cutting off the flow of blood. This condition may result in the death of tissue. If the thrombus dislodges and free floats, it is known as an embolus. Blood clots often develop due to atrial fibrillation (see above), heart valve replacement, a recent heart attack, extended periods of inactivity, and deficiencies of the blood’s clotting abilities due to genetic or medical diseases. Female birth control hormones have also been linked to the increased formation of blood clots. Treatments are used to prevent the formation and growth of existing clots, allowing them to shrink and dissolve on their own.

COMPANY	PRODUCT	PHASE	
Portola Pharmaceuticals, Inc.	Oral Factor Xa Inhibitor	II	Blood Clot

Cardiovascular Diseases

Cardiovascular disease refers to many diseases involving the heart and/or associated blood vessels. These diseases are often referred to as atherosclerosis (arterial disease). There are many forms of the disease, two of which are described below.

Coronary artery disease occurs when plaques of fat, calcium, cholesterol, and other products form deposits in the arteries and prevent the flow of blood to the heart. This results in the heart working harder than normal and often leads to angina. A myocardial infarction (heart attack) occurs when a plaque ruptures and forms a blood clot that blocks the whole artery, causing the portion of the heart fed by the artery to die. The condition can be fatal the dead tissue is large enough. If the patient survives, congestive heart failure (the inability of the heart to pump sufficient amounts of blood through the body) usually results.

Peripheral arterial disease is when an obstruction occurs in the arteries of the arms or legs. Initially, patients feel pain in the affected area. Tissue death and gangrene can ensue if the condition is not treated.

There are many risk factors that can lead to cardiovascular disease later in life: age, nutritional deficiencies, diabetes, hypercholesterolemia, smoking, high blood pressure, obesity, inactivity, and being male. Aside from gender, many of these factors can be controlled and prevented from an early age. Coronary artery disease is the number one killer of both men and women in America, affecting 13 million people and claiming nearly 500,000 lives each year.

	COMPANY	PRODUCT	PHASE
Congestive Heart Failure	CV Therapeutics, Inc.	Adentri / BG9928	II
Peripheral Vascular Disease	Angiogenix, Inc.	Angx1039	II
	Pharmacyclics, Inc.	Antrin (motexafin lutetium)	II
	Valentis, Inc.	Deltavasc	II
Congestive Heart Failure	Titan Pharmaceuticals, Inc.	DITPA	II
Coronary Artery Disease	BioCardia, Inc.	Gene Therapy	II
Congestive Heart Failure	BAS Medical, Inc.	Relaxin	II
	PDL BioPharma, Inc.	Ularitide	II
Peripheral Arterial Disease	Valentis, Inc.	VLTS-934	II
Peripheral Arterial Occlusion	Nuvelo Inc New	Alfimeprase	III
Cardiovascular Diseases	Arginox Pharmaceuticals, Inc.	Tilarginine Acetate Injection (TAI)	III
Coronary Artery Disease	CV Therapeutics, Inc.	Aceon (perindopril erbumine)	M
Congestive Heart Failure	Johnson & Johnson	Natrecor (nesiritide)	M
Peripheral Arterial Disease	Impax Laboratories, Inc.	Pentoxifylline Extended Release Tablets	M
Cardiovascular Diseases	Endomatrix, Inc.	Provasca / Actothil	M

Cardiopulmonary Bypass Surgery

In open heart surgery, the heart and lungs are often bypassed. Blood returning to the heart is diverted through a heart-lung machine (a pump oxygenator) before returning it to the arterial circulation. The machine does both the work of the heart (pumps blood) and the lungs (supplies oxygen to red blood cells).

	COMPANY	PRODUCT	PHASE
Cardiopulmonary Bypass Surgery	XOMA Ltd	Neuprex (opebecan)	II

Coronary Artery Bypass Graft Surgery

More generally known as heart bypass, coronary artery bypass graft surgery is a surgical procedure performed on patients with coronary artery disease to relieve angina and possibly improve the function of the heart muscle. Veins and arteries from the patient’s body are grafted from the aorta to the coronary arteries. The narrowed coronary arteries are bypassed, improving the blood supply to the heart. The American Heart Association estimates that most patients who receive the surgery live 10-15 years longer.

COMPANY	PRODUCT	PHASE	
Lumen Therapeutics	LT-1951	II	Coronary Artery Bypass Graft Surgery

Hypercholesterolemia (High Cholesterol)

Hypercholesterolemia literally means “high blood cholesterol” and is characterized by the presence of high levels of cholesterol in the blood. It is not considered a disease, though it is a metabolic abnormality that can accompany many other diseases, most often cardiovascular disease. Over time, elevated levels of cholesterol in the blood can lead to atherosclerosis and a number of other cardiovascular diseases such as angina, heart attack, strokes, and peripheral artery disease. Those diagnosed with this condition should work to reduce blood cholesterol through diet and exercise. Simple carbohydrates and trans fats should be entirely avoided. In the United States, approximately 101 million people, or 37 percent of the population, have high cholesterol.

COMPANY	PRODUCT	PHASE	
Titan Pharmaceuticals, Inc.	DITPA	II	Hypercholesterolemia
Impax Laboratories, Inc.	Fenofibrate	M	

Hypertension (High Blood Pressure)

In the United States, 65 million adults have hypertension, or high blood pressure. Often called “the silent killer,” it has no symptoms, and left uncontrolled, can have deadly consequences such as heart attack, stroke, and kidney failure. There are many risk factors for high blood pressure, including stress, consuming too much salt or too much alcohol (more than 1 or 2 drinks per day), being overweight, and not getting enough cardiovascular exercise. For many people, there may be a genetic component as well. Having your blood pressure checked by a physician is an easy way to ensure that high blood pressure does not go undetected.

COMPANY	PRODUCT	PHASE	
BioMarin Pharmaceutical, Inc.	6R-BH4 (sapropterin dihydrochloride)	II	Hypertension
CV Therapeutics, Inc.	Aceon (perindopril erbumine)	M	
PDL BioPharma, Inc.	Cardene I.V. (nicardipine hydrochloride)	M	

Hypotension (Low Blood Pressure)

Most people know the dangers of high blood pressure, but few know that when your blood pressure drops too low it can be dangerous as well. When this happens, not enough blood reaches your organs, causing them to not receive enough oxygen and nutrients from the blood. This may cause the organ to not function properly. There are many causes of hypotension, from alcohol, diuretics or other medications, to dehydration, anaphylaxis (severe allergic reaction), or heart attack.

	COMPANY	PRODUCT	PHASE
Hypotension	Impax Laboratories, Inc.	Midodrine Hydrochloride Tablets	M

Myocardial Infarction (Heart Attack)

Heart attack is a disease that occurs when the blood flow to part of the heart is interrupted, causing the death of heart tissue. Generally this is caused by atherosclerosis, the build-up of plaque deposits in the arteries. Occasionally, these fatty deposits burst, causing blood clots to form. These clots block blood from flowing to the heart, and the oxygen-deprived muscle quickly becomes damaged and heart attack ensues.

Symptoms include severe chest pain and general feelings of sickness, sweating and paleness. It is considered a medical emergency and professional care should be sought immediately. A physician will usually give oxygen, aspirin and pain relief initially as a diagnosis is made. An electrocardiogram (EKG) and blood tests will be taken to confirm the heart attack. Treatment generally includes a combination of medication, angioplasty or bypass surgery. More than 1.2 million Americans will have a heart attack this year.

	COMPANY	PRODUCT	PHASE
Myocardial Infarction	KAI Pharmaceuticals, Inc.	KAI-9803 / CS-9803	II
	Genentech, Inc.	Activase (alteplase)	M
	Novartis, AG.	Cardioxane (dexrazoxane)	M
	PDL BioPharma, Inc.	Retavase (reteplase)	M
	Genentech, Inc.	TNKase (tenecteplase)	M

Stroke

A stroke is an acute neurological injury in which the blood flow to a part of the brain is interrupted. There is a sudden loss of neuronal function due to a disturbance of blood flow to the arteries. The part of the brain that does not receive enough blood becomes starved of oxygen and brain cells become seriously damaged or die. This impairs local brain function. Stroke is considered a medical emergency because permanent neurological damage or death can occur if treatment is not sought quickly.

Stroke is the third leading cause of death and adult disability in the United States and Western Europe. According to the American Heart Association Heart Disease and Stroke Statistics 2005 Update, about 700,000 Americans will have a stroke this year. That is one every 45 seconds. Risk factors include old age, hypertension, diabetes, high cholesterol, and smoking. African Americans, American Indians, Alaska Natives, and Mexican Americans have a higher than average risk and recent studies show that women during and after pregnancy also have a higher risk.

	COMPANY	PRODUCT	PHASE
Stroke	Renovis, Inc.	Cerovive / NXY-059 (disufenton sodium)	III
	Neurobiological Technologies, Inc.	Viprinex (ancrod)	III
	Genentech, Inc.	Activase (alteplase)	M

Melissa – A Stroke Survivor Story

I'm only 16, you know I never even thought about having a stroke. To be honest I knew almost nothing about it. It was Christmas vacation and I had a job working at a local department store. I was dizzy and lightheaded and the next thing I knew I was on the floor.

One of my co-workers found me and rushed me home. I remember I couldn't speak and that was really hard because I couldn't explain what was happening. I felt numb and shaky and my vision was blurry. My family called for an ambulance and they took me to the local hospital. They told me I was having a stroke. They put me in the helicopter and took me to UCSF in San Francisco. That's where they used the Merci[®] Retriever to remove my clot.

My friends all ask me what it's like to come so close to death. The thing is I wasn't really scared at all because I didn't know how serious it was/ It all happened so fast and I was okay the next day – it's pretty cool.

Peninsula Stroke Association (PSA) is a Palo Alto based, not-for-profit organization with the mission to educate the public about stroke and to provide support for stroke survivors and their caregivers in San Mateo and Santa Clara counties.

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