



Metabolic Disorders

The endocrine system is an electrochemical connection from the hypothalamus of the brain to the organs of the body that control metabolism, growth and development, and reproduction. It is made up of organs called glands, which secrete chemicals called hormones. Hormones are messengers that travel throughout the body via the bloodstream, affecting other processes and pathways. Typical glands of the endocrine system include the pituitary, thyroid, and adrenal glands. The metabolic pathway is influenced by the endocrine system. It involves the building and breaking down many of the molecules that the body uses, consumes, and produces. The endocrine system is involved in nearly every internal process, from digestion to growth to the balance of fluids and nutrients in the body.

Acromegaly

Acromegaly is a hormonal disorder resulting from the excess production of growth hormone by the pituitary gland. Most often, it is a benign growth hormone producing tumor composed of distinct cells called somatrophs, and is called pituitary adenoma. This disorder most commonly affects middle-aged adults and results in serious illness or death due to its slow progression and difficulty to diagnose. Symptoms include the swelling of hands and feet, protrusion of the brow and lower jaw, arthritis, spacing of the teeth, heart failure, vision loss, diabetes, hypertension, and increased sweating. Treatment includes surgery for removal of the pituitary tumor, radiation, and drug therapy. According to the National Institute of Diabetes and Digestive and Kidney Diseases, three out of every 1 million people will develop the disorder.

	COMPANY	PRODUCT	PHASE
Acromegaly	Tercica, Inc.	Somatuline Autogel (lanreotide)	III
	Nektar Therapeutics	Somavert (pegvisomant)	M

Addison's Disease

Also known as chronic adrenal insufficiency, Addison's disease is a rare endocrine disorder that develops after the adrenal glands, located above the kidneys, do not produce enough of the hormones cortisol and aldosterone. One of cortisol's major functions is maintaining the balance of salt and water in the body. Symptoms include fatigue, weakness, loss of appetite, nausea, diarrhea, vomiting and low blood pressure—all due to a lack of salt in the body. This disease often goes undiagnosed because the symptoms are mild and develop slowly. Rarely, "Addisonian crisis" occurs, during which the symptoms become severe quickly, usually due to another pre-existing illness. If left untreated, Addison's can become fatal. Only 1 in 100,000 Americans is diagnosed with this disease, but may be an inaccurate number due to the difficulty of diagnosis.

	COMPANY	PRODUCT	PHASE
Addison's Disease	Impax Laboratories, Inc.	Fludrocortisone Acetate	M

Appetite

In order for our bodies to function, we need calories and nutrients obtained from the food that we eat. For most of us, this is not a problem. Our bodies give us signals (such as hunger pangs) to let us know that is time to eat. Our appetite is regulated closely by our brain, digestive tract, and adipose (fat) tissue. Many disorders, both biological and psychological, exist in which appetite regulation is abnormal. This can lead to diseases such as anorexia and bulimia where too little food intake occurs and obesity where too much food is consumed. Many therapies exist to help our bodies regulate and control our food intake.

	COMPANY	PRODUCT	PHASE
Appetite	Pherin Pharmaceuticals, Inc.	PH284	II

Diabetes

Insulin is a hormone that our body needs to regulate the amount of sugar in our cells. Sugar is vitally important as it is the primary source of energy for our bodies. Diabetes is a disease in which the patient's body either does not produce or improperly produces insulin, causing sugars to build up in the blood. Because the sugars are not being transferred into the cells, cells are unable to operate as efficiently. Cellular functions rely on glucose sugar as their main

sources of energy. If diabetes is left unchecked it can lead to stroke, cardiovascular disorders, blindness, kidney failure, amputations, and nerve damage. In severe situations, a person can fall into a diabetic coma, known as diabetic ketoacidosis.

There are three types of diabetes which affect 18.2 million Americans. Type I diabetes is an autoimmune disease in which the body's immune system turns against its own cells. The insulin producing beta cells in the pancreas are attacked, causing insulin to be produced at an inefficient rate or not at all. Doctors do not yet know the cause of type I diabetes, though the environment, genetics, and viruses may be a factor.

Type II diabetes is the most common form of the disease. It is associated with being overweight, inactivity, older age, history of gestational diseases, ethnicity, and family history. Insulin is produced normally at first, but the body's cells become resistant to it and do not use the insulin correctly. Eventually, insulin production will decrease as cells receive signals that they do not use as much.

Type III is known as gestational diabetes and only occurs during pregnancy. It is associated with ethnicity and family history. Only about 135,000 people have gestational diabetes at any given time. It is thought to be caused by increased hormone levels, which create an insulin resistance similar to that found in Type II diabetes.

COMPANY	PRODUCT	PHASE	
BEXEL Pharmaceuticals, Inc.	BLX-1002	II	Type II Diabetes
DiObex, Inc.	DIO-902	II	
Perlegen Sciences, Inc.	MCC-555	II	
Plexxikon, Inc.	PLX204	II	
SuperGen, Inc.	PZG (pyrazinoylguanidine)	II	
SuperGen, Inc.	RF 1051	II	Diabetes
Amgen, Inc.	T131	II	Type II Diabetes
Aradigm Corp.	AERx insulin Diabetes Management System / NN1998	III	Type I Diabetes
Aradigm Corp.	AERx insulin Diabetes Management System / NN1998	III	Type II Diabetes
Metabolex, Inc.	MBX-102 (metaglidase)	III	
Impax Laboratories, Inc.	Metformin HCl Extended Release Tablets	A	
Nektar Therapeutics	Exubera (inhaled insulin)	M	Diabetes
DepoMed, Inc.	Glumetza / Metformin GR (metformin hydrochloride)	M	Type II Diabetes
Novartis AG	Novolin	M	Diabetes

Homocystinuria

Homocystinuria is an inherited metabolic disorder in which the amino acid methionine is not properly metabolized. It is an inherited autosomal recessive trait, which means that the child must inherit the defective gene from both parents. Over time, this defect causes a multisystemic

disorder of the connective tissue, muscles, CNS, and cardiovascular system due to the accumulation of homocysteine in the serum and an increased excretion of homocysteine in the urine. It is difficult to diagnose at birth; infants look completely normal and symptoms may or may not be present.

Symptoms include family history of the disease, nearsightedness, flushed cheeks, tall, thin build, long limbs, high arched feet, knock knees, mental retardation, and psychiatric disease. The average life expectancy is reduced only if left untreated, but 25 percent of patients tend to die before the age of 30 due to heart complications. There is no cure for this disease but patients sometimes respond to treatment with vitamin B6. For those patients who do not respond to B6, a low methionine diet is required, with added folic acid and cysteine in the diet.

	COMPANY	PRODUCT	PHASE
Homocystinuria	Jazz Pharmaceuticals	Cystadane (betaine anhydrous)	M

Hypoglycemia

Hypoglycemia refers to a lower than normal amount of glucose (sugar) in the blood. Usually the condition is mild and can be treated by the intake of sugar, but in chronic cases the brain will not receive enough glucose, resulting in impaired function. This can lead to permanent brain damage or death if left untreated. Symptoms include shakiness, anxiety, nervousness, tremor, palpitations, sweating, coldness, hunger, nausea, fatigue and personality changes. Hypoglycemia can occur at any age and from a variety of causes, however, it commonly results as a complication from diabetes. Physicians do not agree as to what level of glucose in the blood classifies hypoglycemia, though glucose levels below 70 mg/dl are generally considered hypoglycemic. Treatments are specifically fashioned after the cause of the abnormality is discovered.

	COMPANY	PRODUCT	PHASE
Hypoglycemia	DiObex Inc.	DIO-901 (glucagon)	II

Growth Hormone Deficiency

Growth hormone deficiency is a condition in which the human growth hormone (HGH) is inadequately produced. Growth hormone, also known as somatotropin, is a polypeptide hormone that stimulates growth and cellular reproduction. At various stages of life, different symptoms and effects may be present. Infants may exhibit hypoglycemia or micropenis. Children will experience stunted growth. Adults may have decreased lean body mass, poor bone density and several physical and psychological problems. HGH deficiency can be either congenital (acquired before the child is born) or acquired in adult life, often by a tumor. It is sometimes temporary, but is most often permanent. HGH deficiency is treated by growth hormone replacement therapy.

	COMPANY	PRODUCT	PHASE
Growth Hormone Deficiency	Tercica, Inc.	Increlex (mecasermin [rDNA origin] injection) / rhIGF-1	III
	Tercica, Inc.	Increlex (mecasermin [rDNA origin] injection) / rhIGF-1	M
	Genentech, Inc.	Nutropin [somatotropin (rDNA origin) injection]	M
	Genentech, Inc.	Nutropin AQ [somatotropin (rDNA origin) injection]	M
	Genentech, Inc.	Nutropin AQ [somatotropin (rDNA origin) injection]	M
	Genentech, Inc.	Nutropin [somatotropin (rDNA origin) for injection]	M

Hormone Replacement Therapy

Hormone replacement therapy is used on perimenopausal and postmenopausal women to prevent discomfort and health problems caused by the diminished estrogen hormones in the body. Treatment involves a series of drugs designed to artificially boost hormone levels. Estrogen, progesterone, progestin, and testosterone are the main hormones involved.

COMPANY	PRODUCT	PHASE	
Berlex	Androgen/progestin Replacement Therapy	II	Hormone Replacement Therapy

Idiopathic Short Stature

Idiopathic short stature (ISS) refers to the condition of someone being shorter in height than those around them. Height, however, is a relative condition, and there are no established definitions as to what is a “normal” height. There have been several controversies over this issue regarding quality of life due to height and insurance reimbursement for hormone therapies and treatments.

COMPANY	PRODUCT	PHASE	
Genentech, Inc.	Nutropin AQ [somatropin (rDNA origin) injection]	M	Idiopathic Short Stature
Genentech, Inc.	Nutropin [somatropin (rDNA origin) injection]	M	

Obesity

Obesity is a condition in which the natural fat stores in the body are increased to the point where it is a risk factor for health conditions or increased mortality. A body mass index (BMI) between 30.0 and 39.9 classifies a person as obese. In men, this means that when body fat is greater than 25 percent and in women when fat is over 30 percent, the patient is declared obese. Excess body weight is linked to genetics, overeating, lack of exercise, as well as certain diseases such as cardiovascular disease, diabetes, sleep apnea, and osteoarthritis. Stress, eating disorders, and smoking cessation may also contribute to the condition.

Obesity is quickly becoming a substantial public health problem and it significantly contributes to rising health care costs in the United States. According to a recent study by the Centers For Disease Control and Prevention, the United States has the highest rate of obesity in the developed world. From 1980 to 2002, obesity in the U.S. doubled in adults and tripled in children and adolescents. From 2003-2004, 17.1 percent of children and adolescents aged 2 to 19 years, and 32.2 percent of adults 20 years or older were obese. The prevalence of obesity has been continually rising due to environmental and population factors that support decreased physical activity and increased calorie consumption.

COMPANY	PRODUCT	PHASE	
VIVUS, Inc.	Qnexa	II	Obesity
SuperGen, Inc.	RF 1051	II	

Testosterone Replacement Therapy

Testosterone is a steroid hormone primarily secreted in the testes of males and the ovaries of females. The adrenal glands also secrete small amounts of the hormone. It is the principal male sex hormone and an anabolic steroid that plays major roles in health and well-being. Libido, energy levels, immune function, protection against osteoporosis, and puberty in males are largely due to increased levels of testosterone in the body. In some individuals, however, the production of testosterone is insufficient for the healthy growth and development of the body. In these cases, hormone replacement therapy is used to maintain normal levels of testosterone in the body.

COMPANY	PRODUCT	PHASE	
Impax Laboratories, Inc.	Methitest CIII (methyltestosterone)	M	Testosterone Replacement Therapy
Pharmagenesis, Inc.	Testoderm TTS	M	

