



## Amgen and Biovitrum Expand Existing License Agreement for Innovative Treatment of Type 2 Diabetes and Other Metabolic Disorders

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THOUSAND OAKS, Calif. & STOCKHOLM, Sweden--(BUSINESS WIRE)--Feb. 13, 2006---Amgen (NASDAQ:AMGN) and Biovitrum AB today announced that they have expanded their existing agreement under which Amgen will now receive exclusive worldwide rights to develop and commercialize Biovitrum's small molecule 11beta-HSD1 enzyme inhibitors for the treatment of metabolic diseases and certain other medical disorders. The most advanced compound in this collaboration is currently in early clinical development.

The original development and marketing collaboration agreement, announced in September 2003, provides Amgen the exclusive right to commercialize products in North and South America, the European Union, Australia and New Zealand. Under the expanded agreement, Amgen receives exclusive worldwide rights to commercialize all developed products, while Biovitrum retains co-promotion rights in the Nordic region for all products developed.

Amgen will pay an undisclosed amount for the upfront payment related to the expanded licensed territory. Amgen will also fund and conduct all further development and commercialization activities worldwide. Biovitrum may receive additional milestone payments related to development progress and regulatory submissions for metabolic diseases. Once a product has been approved, Biovitrum will receive tiered royalties on future worldwide sales of all products arising from the agreement.

"Amgen continues to believe that this collaboration with Biovitrum will move us toward discovering innovative treatments for type 2 diabetes and related metabolic diseases," said Will Dere, M.D., senior vice president of Global Development and chief medical officer at Amgen.

"Amgen has proven to be an excellent partner for our 11beta-HSD1 enzyme inhibitor program and we are very happy to expand this collaboration," said Mats Pettersson, CEO of Biovitrum. "We are confident that Amgen will remain a strong and committed partner for completing development of this innovative approach for helping those suffering from type 2 diabetes and related disorders," commented Mats Pettersson.

Type 2 diabetes, a disease in which insulin resistance leads to elevated blood sugar levels, currently afflicts over 160 million people worldwide. Approximately 20 million Americans currently suffer from type 2 diabetes. Early intervention using innovative therapies has the potential to delay the onset of life-threatening metabolic disorders.

### About Amgen

Amgen discovers, develops and delivers innovative human therapeutics. A biotechnology pioneer since 1980, Amgen was one of the first companies to realize the new science's promise by bringing safe and effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, and other serious illnesses. With a broad and deep pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. To learn more about our pioneering science and our vital medicines, visit [www.amgen.com](http://www.amgen.com).

### About Biovitrum

Biovitrum is one of the larger biopharma companies in Europe. With operations in Sweden and in the UK Biovitrum conducts research and develops pharmaceuticals for both broad diseases and conditions that affect smaller patient populations. Biovitrum focuses on drugs for the treatment of obesity, diabetes, inflammation and blood diseases as well as a number of well defined niche indications. Biovitrum develops and produces protein-based drugs on a contractual basis and markets a range of specialist pharmaceuticals primarily in the Nordic countries. Biovitrum has approximately 500 employees. For more information see [www.biovitrum.com/](http://www.biovitrum.com/).

### 11beta-HSD

Excess glucocorticoids such as cortisol produce visceral obesity and diabetes. 11beta-hydroxysteroid dehydrogenases (11beta-HSDs) are enzymes that play an important role in the interconversion of glucocorticoids between the active and inactive forms. Two enzymes have been identified, 11beta-HSD1, and 11beta-HSD2. These 11 beta-HSDs play a major role in the modulation of local cortisol levels and the access of active steroid to its receptors in the target tissues. Thereby, the 11beta-HSDs are also believed to have important roles in a number of common diseases, including obesity, type 2 diabetes and hypertension.

11beta-HSD2 is found primarily in tissues such as kidney, sweat glands and salivary glands. 11beta-HSD2 converts active glucocorticoids into inactive steroids and appears to act as an effective barrier to excess cortisol across a wide range of cortisol concentrations. However, in studies where the 11beta-HSD2 enzyme activity has been inhibited with liquorice this results in an excess of steroids that cause hypokalemia and hypertension.

11beta-HSD1 is present in tissues of importance for metabolism and insulin sensitivity such as the liver and the adipose tissue. Its activity can be altered by factors such as glucocorticoids, stress, sex steroids, growth hormone, cytokines and PPAR agonists. Under normal conditions, 11beta-HSD1 is believed to amplify local glucocorticoid concentrations in target tissues, in particular when the circulating plasma cortisol levels are low. However, in obese subjects the levels of 11beta-HSD1 are usually markedly increased, at least in adipose tissue. This observation is of importance in the light of a rodent study recently published in Science, demonstrating that animals with an increased 11beta-HSD1 activity (i.e. transgenic animals) have an excess of visceral fat and are insulin resistant, diabetic and dyslipidemic. Furthermore, in humans, pharmacological inhibition of 11beta-HSD1 with non-selective compounds has previously been shown to result in enhanced insulin sensitivity. This finding indicates that 11beta-HSD1 appears to play an important role in type 2 diabetes and the metabolic syndrome also in man, and that selective inhibitors of 11beta-HSD1 could become a very useful tool in the treatment of this disorder.

Type 2 Diabetes (also known as non-insulin dependent, adult onset or type 2 diabetes mellitus)

Type 2 diabetes is a lifestyle disease with a strong hereditary component. Estimates of diabetes prevalence around the world have more than tripled since 1985. The current global prevalence is approximately 160 million people and has been estimated to increase to 300 million people in 2025. Presently, approximately 6 percent of the population in the United States is diabetic. Of these patients, 90-95 percent are afflicted with different forms of type 2 diabetes, a condition that is expected to become increasingly widespread, due to the increasing number of elderly, a more sedentary lifestyle and rapidly growing incidence of obesity. The worldwide annual average mortality in diabetics (5.4 percent) is twice as high as in non-diabetics. Each year in the United States alone type 2 diabetes results in about 200,000 deaths, 400,000 heart attacks, 130,000 strokes, 60,000 amputations, 10,000 new cases of kidney failure requiring dialysis or transplantation and 6,000 new cases of blindness. Type 2 diabetes also leads to other disabilities, especially nerve damage, that could result in erectile dysfunction, numbness, intractable nausea, and diarrhea. Diabetes is currently the sixth leading cause of death by disease in the United States and is estimated to cost the U.S. health care system 100 billion USD per year. It is estimated that by the year 2010, diabetes will exceed both heart disease and cancer as the leading cause of death through complications.

Type 2 diabetes is a progressive disease caused by a combination of decreased tissue sensitivity to insulin (insulin resistance) and an insufficient insulin secretion. The blood glucose control in type 2 diabetes usually deteriorates over time and, despite lifestyle intervention efforts, additional pharmacological treatment in many cases ultimately becomes necessary. Type 2 diabetes is frequently associated with obesity, dyslipidemia, hypertension, atherosclerosis, thrombosis and cardiovascular disease. In the treatment of diabetes it is important to address all these aspects of the disease. The unmet need for new, safe and effective treatment tools to prevent the progression of the type 2 diabetes, its serious complications and the associated over-mortality in this disease remains enormous.

EDITOR'S NOTE: An electronic version of this news release may be accessed via our Web site at [www.amgen.com](http://www.amgen.com). Journalists and media representatives may sign up to receive all news releases electronically at time of announcement by filling out a short form in the Media section of the Web site.

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