

Executive Summary

Obesity has reached epidemic proportions in industrialized countries, especially the United States, and is rapidly increasing in prevalence worldwide, particularly in emerging economic powers such as India and China. With the increase in prevalence of obesity comes an increase in its co-morbidities, especially type 2 diabetes (which has also reached epidemic proportions) and cardiovascular disease.

Although obesity has traditionally been thought of as being due to a lack of “personal responsibility” or willpower, basic research shows that it is a disease that is driven by genetic, behavioral, and environmental factors. Obese or overweight individuals who attempt to lose significant amounts of weight fight a set of physiological factors that were designed to ward off starvation in our evolutionary past, and that have become dysfunctional in an age of abundant, cheap food and socioeconomic factors that discourage exercise and healthy eating habits. These social and economic changes are driving up the average weight of populations in country after country, with obese individuals falling at the top of the curve. Although many individuals have managed to lose significant amounts of weight via diet and exercise (and especially the loss of 5% to 10% of body weight, which wards off obesity’s co-morbidities), long-term weight regain, often with more weight gained than was originally lost, is the rule.

The above factors indicate that obesity drugs will be necessary, in addition to diet and exercise, to combat obesity, both on an individual and a population basis. However, the few drugs that are currently approved for long-term treatment of obesity are only marginally effective, and have significant adverse effects that limit their use. Clearly, new drugs are needed. However, it has been difficult to successfully develop obesity drugs, because of the complexity and inadequate knowledge of pathways that control energy balance in

the human body, notable safety failures of several late-stage and marketed obesity drugs (such as the notorious case of Fen-Phen [fenfluramine/phentermine]), and the continuing perception that obesity is a “lifestyle” issue rather than a disease.

After a review of the physiology and genetics of obesity, and the factors that make development of obesity drugs difficult, this report focuses on the pipeline of Phase III and Phase II drugs that are under development in the biotechnology and pharmaceutical industry, their mechanisms of action, and the clinical evidence for their efficacy and safety. Drugs discussed include VIVUS Pharmaceuticals' Qnexa (phentermine/topiramate), Orexigen Therapeutics' Contrave (bupropion/naltrexone) and Empatic (zonisamide/bupropion), Arena Pharmaceuticals' lorcaserin, Alizyme's cetilistat, and several others. The report then goes on to explore leading early-stage approaches to developing succeeding generations of obesity drugs.

The report also includes the results of a survey of researchers and executives in corporate and academic organizations whose work involves discovery and development of obesity drugs. The survey results include information on the involvement of the respondents in obesity drug R&D programs and their views on the current state of the field and its future potential.

Finally, the Appendix includes expert interviews with four industry leaders: Olivier Boss, PhD, of Sirtris; Alice Izzo of Amylin Pharmaceuticals; Peter Tam of VIVUS; and David Walsey of Arena Pharmaceuticals.