

What Investors Should Know about Obesity

Obesity is a growing global epidemic. An estimated 30% of the US population considered obese with 6% severely or morbidly obese. The combined comorbidities of obese patients is regarded as biggest single drain on the US healthcare system, estimated over \$200 billion a year in the United States. The reasons are numerous and complex and the costs are significant. A recent McKinsey report ranked obesity as the third biggest cost to Global Domestic Product (GDP):

- Smoking, \$2.1 trillion
- Armed Violence, War and Terrorism \$2.1 trillion
- **Obesity \$2.0 trillion**
- Alcoholism \$1.4 trillion

Few treatments. Few approved drugs. Massive market.

Drugs vs. Devices. The two approaches for treating the severe or morbidly obese are surgical interventions and drug therapies. An estimated **18 million people in the US are candidates for** (bariatric) surgery, yet only a few hundred thousand undergo surgical procedures each year. This is due ineligibility, post-surgical complications such as mortality, and substantial costs. Costs range from \$17,000 to \$35,000. There is no FDA-approved therapeutic alternative (drug) that demonstrates the efficacy of surgery. This article focuses on the low hanging fruit of addressing the 6% of the US population severely or morbidly obese.

The Fen – Phen Effect. Ever since the Phen-Fen debacle in the late 90’s, there has been a dearth of new drug approvals. After 13 years of no drug approvals, 4 drugs became approved recently. It is not surprising that the FDA and drug developers have been careful to approve an obesity drug. When the Mayo Clinic reported permanent rare heart disease from the use of Fen-Phen, Wythe had it pulled from market, making there a \$21 billion legal expense. Pfizer then acquired the company.

Relatively Uncrowded. Competitive environment makes this area attractive, because there are so few drugs in development. There are hundreds of drugs being developed for cancer, while our [Global Report](#) identified just 11 in Phase I, II, or III for obesity. Big market with few players currently.

Market opportunity. This is a massive market. Some call it the “holy grail”, comparing the potential to that of a Lipitor, which generated \$13 billion a year and \$120 billion in revenues over its life. With the massive and growing market, we expect there will be more entrants soon. In its recently completed [Global Obesity Report](#), OneMedResearch identified **32 companies** with obesity drugs in development, **11 drugs** at some stage of the FDA approval (United States only), and **21 distinct drug targets** utilizing **18 mechanisms of action**.

Obesity is the most serious health risk today, yet it is the most underserved market. Patients who are severely obese (BMI>35+), mildly obese (BMI >30~34.9), and overweight (BMI 25~30) must each be treated differently. In 2010, there were 37 million severely obese individuals in the USA. If current trends continue, severe obesity is expected to increase 3 times faster than the rest of the obese population. Therefore, this number is expected to reach 60 million by 2020, and 90 million by 2030. Severe obesity imposes much higher health risks, medical costs, and social costs than mild obesity. There are few treatment options for severe obesity other than gastric surgery. Once severe obese patients reduce their body weight, becoming mildly obese, there may be a wider range of treatment options available including oral drugs, exercise, and diet.

Severe Obesity vs. Cancer. In 2010, the medical costs for cancer and obesity were respectively \$124 billion and \$120 billion in USA.

Marketplace today. The recent additions of Saxenda and Contrave have dampened the performance and growth of surgical procedures. The impact on the market of these two recent launches are too early to tell, but market share as of May 15th 2015 is as follows.

Drug	No. of prescriptions filled		
	Week ending 05/1/15 ¹	Q1 2015	2014 (year-end)
Belviq	14834	169,000 ³²	479,000 ³³⁻³⁶
Contrave	13154	117,193 ³⁷	N/A ²
Qsymia	11675	136,000 ²⁹	534,000 ³⁰
Saxenda	198	N/A ²	N/A ²

How these Drugs Work. Anorexics and Fat Burning

Obesity is an accumulation of excess fat due to energy intake surpassing energy expenditure. Obesity can be treated only when energy expenditure becomes higher than energy intake. So far, the primary approach to treating obesity with drugs is via which suppress appetite or inhibit caloric absorption. Drugs that decrease energy intake include:

- **Centrally acting drugs that suppress appetite:** Most current obesity drugs fall into this space. These include sympathomimetic amines, which have been used in the clinic for over fifty years. Newer drugs in this space include **Qsymia** (2012), **Belviq** (2012) **Contrave** (2014), and **Saxenda** (2014). All these agents work to suppress appetite through different means, thereby leading to decreased food consumption.
- **Peripherally acting drugs that inhibit caloric absorption:** Orlistat is currently the only drug in this space. In addition to prescription strength **Orlistat** (Xenical- approved in 1999), an over-the-counter (OTC) version Alli was approved for sale in the US in 2007. These agents act distally to reduce caloric absorption in the intestine, which decreases overall energy intake.

No drug is approved that reduce weight through increasing energy expenditure. **Drugs that increase energy expenditure:** Fat Burning (increase energy expenditure): With the recent discovery of Brown Adipose Tissue (BAT, or Brown Fat) in human adults, several drugs are being developed.

Brown Fat Discovery: A Breakthrough

Brown Fat. In this last area, drugs that offer the possibility to increase energy expenditure are where the major opportunity lies. In 2009, researchers at Harvard initially looking for cancer, discovered that brown fat exists in adults.

Unlike White Adipose Tissue (WAT) or **white fat** which serves as a storage source of energy, **brown fat** is an *energy burning fat* whose purpose is to generate heat. We've long understood its critical role as the biological tool to provide warmth and consistent body temperature in infants. We thought its role and existed ceased as we moved into adulthood. It wasn't until cancer researchers used advanced imaging systems, and noticed dark spots that were NOT cancers. Rather, they found that these spots were deposits of mineral rich mitochondria in brown fat. Brown fat was rediscovered. This breakthrough is bringing forth an entirely new group of drug developers seeking a blockbuster for Obesity.

Critical Success Factors and Key Considerations

The big key to a blockbuster will occur when a drug can generate a double digit impact on weight. The drugs on the market have hovered around ~5% impact on overall body weight with Saxenda indicating as much as an 8%. An early indication is that fat burning approaches are now showing animal data with a 25% reduction of body weight. Some of the key considerations for investors:

- **Dosing and compliance.** This may be one of the biggest and first questions. How will the drug be administered and how often? Oral vs. injectable? How frequently? Self-administered or a required physician visit? Will there be visits to the clinic every month or as infrequent as six months? This could have a major impact on compliance and therefore, success.
- **Small molecule vs. Peptide vs. Biologics.** The new drugs are taking a variety of approaches. Each approach has its strengths and limitations.
- **Side Effects and regulatory approval.** The Phen Fen experience remains a cloud over the FDA and Pharma. As such safety profiles will affect approval process, and will require more time. One of the primary concerns with safety is the long term side effect. The use of Anorexics in particular impact the CNS system resulting in such side effects as depression. Thus we believe it will likely be some time before a diet drugs will be approved for the merely overweight.
- **Economics and reimbursement.** American Medical Association (AMA) declared this a disease in **2013**, which has had an impact and should continue to improve reimbursement for treatment.

Marketplace tomorrow. It appears that Brown Fat has opened up a new door and could lead to a paradigm shift in obesity drug development. The Global Report identified 7 companies with interesting new approaches, and 11 companies within the regulatory pipeline. We expect more to come into focus including several firms we know to be in “stealth mode”, and at their request (and on agreement that once they were out of stealth mode we would be the first informed) we did not publish summaries.

Firms and Investors to keep an eye on.

Prominent Players. The best known player in this emerging fat burning area is Zafgen which has been considerable success for investors to date. With over \$36 million in venture capital from such firms as Third Rock and Alta Ventures and another \$96 million raised via a 2014 IPO in now has a market capitalization (as of June 20. 2015) nearly \$1 billion. This company has others hopeful they can follow suit. Our recent research report identified 9 other companies with “Zafgen like” ambitions.

The Investors in this space. Third Rock Ventures was the lead in Zafgen, which is by far the most active investor in obesity currently of the 14 active venture funds we analyzed. Alta Ventures also had a big position in Zafgen, which helped Alta earn their status as one of the highest returning venture funds in healthcare. But compared to almost any other therapeutic investment area in healthcare, there are very few active investors at the moment. We expect this to change as these new fat burning technologies proceed to clinic.

For additional information on the Global Obesity Report. Visit www.onemedmarket.com/#!obesity/c18xc

Authored by Brett Johnson, Managing Director of OneMedResearch. Recently supervised a team of PhD's to complete a Global Industry Report on Obesity. The purpose of the report is to give investors an overview of the investment opportunities in emerging growth companies and new pharmacological treatments for Obesity.