



## Small biotechs tackle the big problem

**The statistics speak for themselves. More than half of the US adult population is overweight and 50% of these are obese. Obesity-related conditions account for 300,000 deaths in the US every year, and in 2000, the costs associated with the condition were \$117Bn. Put simply – obesity is an epidemic.**

There are only two drugs available to treat obesity – Roche's Xenical (orlistat) and Abbott Laboratories' (previously Knoll's) Meridia (subitramine; Reductil in the UK). These were much hyped when launched but their sales have been disappointing and patients have suffered nasty side effects. In the case of Meridia, these undesired effects – elevated blood pressure and heart rate – have resulted in Italy recently withdrawing all subitramine products from sale.

Biotech companies are hoping to fill the gap in the market, and there are many drugs in clinical development. These include Regeneron's ciliary neurotrophic factor Axokine, Alizyme's lipase inhibitor ATL-962, and Phytopharm's P57. However, biotech start-ups are jumping onto the obesity bandwagon. Many of them are using the scientific advances resulting from the genomics revolution to look at obesity from different angles. *BVV* reviews a selection of these companies.

### AdipoGenix

Five professors from the Boston University School of Medicine conducting obesity and diabetes-related research founded AdipoGenix. "We met on a bi-weekly basis at a research meeting at the medical school," Professor Steven Farmer, one of the founders, told *BVV*. "It was during one of these meetings...that we considered starting a consultancy and contract research based company whereby we would offer our services to the pharmaceutical industry to provide information concerning the development of assays etc for drug discovery. But in consulting with various individuals familiar with start-ups, it became clear that we were in a position

to discover drugs ourselves." The scientists sought the help of Dr Jeff Leighton – now AdipoGenix' managing director – who had recently started his own company in Boston, called BioDesign, aimed at helping start-ups get off the ground. AdipoGenix began operations in July 1999.

AdipoGenix is focused on discovering drugs that target the fat cell and inhibit the accumulation of fat in adipose tissue. "We are developing several different HTP screens to find drugs that affect different aspects of the function of the fat cell," explains Farmer. "AdipoGenix has a close working relationship with surgeons at the Boston Medical Center, and we have been able to obtain adipose tissue... We probably have the world's largest repository of human fat cells." AdipoGenix screens for drugs that affect different properties of the different types of fat cells. "We have screened many thousands of chemical entities... We have several hits and a couple of them have been tested in secondary screens that allow us to consider them as potential leads. These screens are designed to determine the mechanisms by which these chemicals block fat uptake in the human cell."

Farmer believes that by targeting the fat cell, AdipoGenix differs from existing companies addressing obesity. "Most companies thought that adipose tissue was a passive player, simply storing fat and releasing it in response to nutritional requirements. Therefore, they focused either on the CNS or GI tract," where side effects are more prevalent, says Farmer. Other companies are beginning to appreciate the role of the fat cell. "We have had many conversations with our colleagues in big pharma who are now interested in our strategy," concludes Farmer.

### ObeTherapy Biotechnology

Dr Itzik Harosh founded ObeTherapy Biotechnology, based at the Genopole biotech incubator near Paris, France, two years ago. The company received seed capital from Genopole, CRITT chimie, Conseil Regional De l'Ile

De France, and a business angel. It is yet to have its series A funding round.

ObeTherapy's approach is different from the vast majority of companies studying obesity: it studies slim people. Specifically, it looks at individuals who are hypocholesterolaemic and have problems with absorbing fatty acids. "That means they can eat almost as much as they want since they are inefficient at fat absorption. These individuals are rare because during evolution they have been eliminated as they did not have an advantage. Nowadays they do have an advantage – compared to us," explains Harosh. In particular, ObeTherapy is interested in mimicking heterozygotes, i.e. individuals who absorb fat inefficiently but do absorb it partially. These individuals are healthy. Homozygotes – individuals who have zero absorption – are very ill and suffer from severe diarrhoea. "We want to develop a drug that will partially inhibit fatty acid absorption," says Harosh. "For us the key thing is to mimic the heterozygote." By doing this, ObeTherapy believes it can create a drug without the severe side effects seen with current therapies.

ObeTherapy has identified several candidate genes and has completed a proof-of-concept test for one of these. Furthermore, in collaboration with Pharmacopeia subsidiary Accelrys, it has a rational drug design programme which has identified a number of hits. ObeTherapy is aiming for one of these to enter Phase I within a year, says Harosh.

### Lipomics Technologies

Lipomics Technologies, based in West Sacramento, CA, was founded in May 2000. Rather than developing its own therapies, it is developing a database to help other companies to do so. Dr Steve Watkins, co-founder and president, became aware of the market for such technology whilst working at the University of California at Davis. "It was at the time when genomics and genomics companies were starting to boom," says Watkins. "We thought that

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