

## Companies throw their weight behind new antiobesity drugs

When diet and exercise alone don't work, people struggling with obesity sometimes turn to weight loss drugs. Existing medications work by altering appetite or fat absorption but can carry nasty side effects such as stroke or severe diarrhea. Now, the US Food and Drug Administration (FDA) is starting to review three drugs—each affecting the brain's appetite centers via slightly different mechanisms—that promise to help people lose 5% of their body weight safely and with few adverse effects. The medications could help curb the world's growing obesity epidemic, but whether the drugs will succeed where many others have failed remains uncertain.

Most pharmaceutical companies have been wary of developing weight loss drugs because past candidate compounds have caused dangerous side effects or have simply proven ineffective, says Harold Bays, medical director of the Louisville Metabolic and Atherosclerosis Research Center in Kentucky who has done company-sponsored research on all three of the newcomer drugs. "Prior to these promising agents, it has often been challenging, to say the least."



**Looming large:** Fat loss drugs aim to carry their weight

Nevertheless, the three small, California-based companies—Orexigen Therapeutics, Vivus and Arena Pharmaceuticals—remain undeterred. All three completed phase 3 trials last year with promising results. Both Arena and Vivus submitted FDA drug approval applications for their drugs in late December, whereas Orexigen is poised to file in the first half of the 2010, the company says.

Although the three drugs have similar modes of action, they may fulfill different niches, notes Louis Aronne, a weight loss

expert at the Weill Cornell Medical College in New York who has worked on all three drugs. Orexigen's Contrave, which combines an antidepressant and an antiaddiction drug, seems to dampen food cravings, whereas Arena's Lorcaserin, a new serotonin receptor stimulant, is designed to create a feeling of fullness. In contrast, Vivus' Qnexa aims to do both by mixing an established weight loss compound with an antiepilepsy drug known to help shed the pounds.

If approved, all three drugs could hit the market within the next 18 months, but the competition that would ensue

doesn't faze Dennis Kim, Orexigen's senior vice president of medical affairs and communications. He says that three is better than one in terms of increasing education and reducing consumers' potential mistrust toward treating obesity with a pill. "Having three companies come together raises the tide," he says. "It's advantageous for everyone in the market."

On the surface, Qnexa seems to hold the most promise—in two clinical trials, subjects on the drug lost a placebo-corrected average of 9% of their body weight, compared to more modest losses observed in separate clinical trials that tested the effects of Lorcaserin and Contrave. But, despite the apparent differences, Bays says that it's an apples-to-oranges scenario. "These are not head-to-head trials," he stresses. "If [the drugs] have all fulfilled the FDA requirements for approval based upon efficacy, then they're even across the board."

Last month, Vivus also reported the results of a phase 2 trial showing that Qnexa lowered the rate of sleep apnea by 69%. Orexigen and Arena have yet to test the effect of their compounds on this breathing disorder.

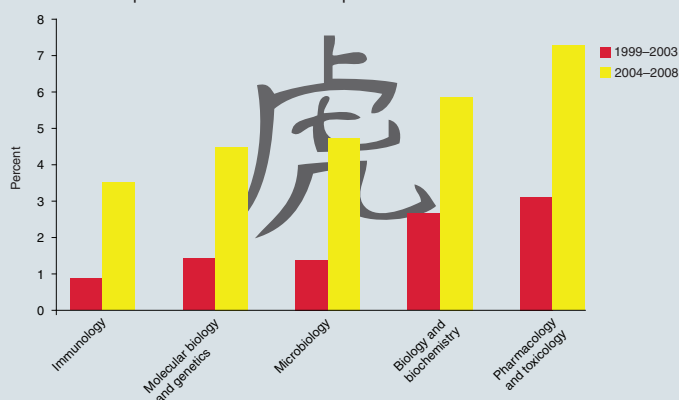
Whether these drugs will work for the population at large remains to be seen. John Speakman, who studies obesity at the University of Aberdeen, UK and was not associated with any of the drugs, notes that the molecular mechanisms controlling appetite also affect many other physiological processes so there may be unforeseen consequences. "The major challenge for the pharmaceutical industry is to develop drugs that capture the food-intake inhibition effects without any side effects," he says. "Given the complexity and interrelatedness of the brain mechanisms involved, that is a significant challenge."

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## China leaps higher in research share

This Chinese New Year is the Year of the Tiger—an appropriate icon for China's increasing strength in the research landscape. A Thomson Reuters study released last November showed the country's research output increasing from over 20,000 papers in 1998 to nearly 112,000 papers in 2008. The Faculty of 1000, an online database of research papers, noted a similar trend in December, with China's articles in PubMed increasing nearly tenfold between 1999 and 2008. However, enthusiasm about the trend might be dogged by reports suggesting that cash incentives to publish may be contributing to misconduct such as plagiarism in China (*Nature* **463**, 142–143, 2010).

China's increasing percentage share of world research publications over two time periods<sup>a</sup>



<sup>a</sup>Data from Thomson Reuters's "Global Research Report: China," November 2009.

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