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Lithera's Phase II Fat Reduction Drug Aims to Follow Botox Model

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Lithera Inc. isn't the only biotech with a generic-drug-combo product designed to bust fat. But unlike the competition, this San Diego start-up is focused not on obesity but on a combination of orphan drug and aesthetic applications similar to the development path pioneered by Allergan Inc.'s Botox (onabotulinumtoxin type A).

Lithera was founded in early 2007 based on research conducted by Frank Greenway, chief of the outpatient clinic at the Pennington Biomedical Research Center at Louisiana State University. Greenway had established the efficacy of adrenergic agents in localized fat reduction, but frequent administrations and slow results made the approach impractical.

John Dobak, serial CEO and founder of the JAKK Group life science accelerator, learned about Greenway's work and had some ideas for improving the efficacy while decreasing the dosing frequency. The result was LIPO-102, a subcutaneous formulation of the generic drugs salmeterol xinafoate and fluticasone propionate.

Salmeterol, a long-acting beta2-adrenergic agonist, stimulates the natural pathway for metabolism of fat, Dobak explained. Fluticasone is a corticosteroid that "up-regulates the machinery that salmeterol turns on," he added.

The two drugs have been combined in an inhaled formulation for the treatment of asthma, but Dobak said Lithera believes it has freedom to operate with its complex subcutaneous formulation.

Several biotechs are pursing combinations of generic drugs for the treatment of obesity. Orexigen Therapeutics Inc.'s Contrave combines long-acting versions of naltrexone, an opioid blocker approved for opioid and alcohol addiction, and bupropion, a dopamine stimulator approved for depression and smoking cessation. The combination is designed to affect the reward pathways associated with food addictions while increasing energy burn.

Orexigen also has Empatic, which combines bupropion with zonisamide, a seizure drug intended to prevent weight gain by inhibiting energy storage and hunger.

There's also Vivus Inc.'s Qnexa, which combines the generic diet drug phentermine with epilepsy drug topiramate to decrease appetite while increasing energy usage and fullness.

Both Contrave and Qnexa are under FDA review for obesity. But Dobak, who serves as Lithera's CEO, explained that LIPO-102 is not targeting obesity. It shrinks fat in a local area, such as the abdomen, but it doesn't cause overall weight loss.

Dobak and Greenway had initially envisioned using LIPO-102 for exophthalmos, an orphan condition associated with thyroid disease in which fat accumulates around the orbit of the eye, causing the eyeball to bulge. The only treatment is surgery. Dose-ranging studies are under way in Australia, and Dobak said the initial feedback has been positive.

Other potential applications for LIPO-102 could include fatty tumors known as lipomas and certain lipodystrophies associated with HIV, in which fat redistributes to form a hump on the back. Lithera is not yet pursuing those indications.

What the company is pursuing, however, is what Dobak refers to as "body contouring." The drug would be given to healthy people who, despite diet and exercise, have a bulge of fat they'd like to get rid of. It's an application where "a lot of snake oil is being sold, if you will, and we'd like to bring a little science," Dobak said.

Phase IIa data released in March showed that the optimal dose of LIPO-102 was well tolerated and reduced mean abdominal circumference by 3.47 cm ($p = 0.017$) after eight weeks.

Data from a second Phase IIa trial released last week showed mean abdominal circumference reductions of 1.2 cm vs. 0.1 for placebo ($p = 0.048$). The effects were sustained for six to 12 weeks.

Dobak said Lithera plans to initiate Phase IIb studies soon and hopes to conduct its end-of-Phase-II meeting with the FDA by late 2011. Lithera plans to pursue a 505(b)(2) pathway for approval.

While insurance providers would likely cover LIPO-102's orphan indications, the body contouring application would be an out-of-pocket expense for patients.

In this way, the business model would be similar to

Botox, which is approved for medical conditions like cervical dystonia pain, eyelid spasms (blepharospasm) and eye muscle problems (strabismus) as well as for cosmetic wrinkle reduction.

Botox garnered $1.3 billion last year. Dobak believes the opportunity for LIPO-102 as an alternative to liposuction surgery in the body-contouring market could be similarly lucrative. He explained that about 150,000 people undergo anti-wrinkle surgery annually, while seven times that amount, or more than 1 million, opt for Botox. Since 350,000 people get liposuction annually, applying the seven-times multiple leads to a LIPO-102 patient population of roughly 2.5 million.

Lithera, a largely virtual operation with 10 employees, has raised $21 million in two rounds of venture capital from Domain Associates and Alta Partners.

The biotech plans to raise a Series C round in the next six to 12 months. Dobak noted that while Lithera is prepared to advance its programs as far as necessary alone, it is also talking to potential partners. ■