

## Press Release

### **Obecure Achieves Successful Results in its Proof of Concept Clinical Study Evaluating the Ability of Histalean™ to Mitigate Weight Gain Associated With Olanzapine**

**Ramat Gan, ISRAEL, June 14, 2009** - Obecure Ltd., a subsidiary of Bio-Light Israeli Life Science Investments Ltd. (TASE: BOLT), announces a positive outcome of its BET-209 clinical study, a randomized, double-blinded, placebo-controlled, four week Phase Ib, Proof-of-Concept (POC) study evaluating both the safety and the ability of Histalean™ to mitigate the weight gain side effect associated with the anti psychotic drug, Olanzapine.

Preliminary analysis showed that the study achieved its primary objective, confirming the safety of administering 144 mg/day Histalean™ (a dose which is three-fold higher than the standard) in combination with Olanzapine. Moreover, top line results indicate a statistically significant reduction in mean weight gain due to Olanzapine in the Histalean™ treatment group, as compared to the Placebo treatment group.

According to Dr. Yaffa Beck, CEO of Obecure, this is an impressive accomplishment and an important step towards providing an appropriate solution to the clinically significant weight gain which is caused not only by Olanzapine, but by a range of second generation antipsychotic drugs with a similar mechanism of action. "Of course, the road towards completion of the clinical development package, which is a prerequisite for marketing approval, still stretches in front of us; however, I believe that these results will enable dialogue with the regulatory authorities, such as the FDA, so as to continue our clinical development program in the USA, Europe, Japan and the rest of the world".

Olanzapine, marketed by Eli Lilly as Zyprexa®, is a highly effective treatment for schizophrenia and bi-polar disorders and is selling about \$4 billion, annually. Yet, like many other atypical antipsychotic drugs, its use is associated with significant side effects that limit its benefit. Most serious is a rapid weight gain (up to 22 Lbs over the initial 16 weeks of treatment) which afflicts a large proportion of the patients and increases their probability to have metabolic diseases such as Diabetes and Cardio-Vascular disease. This is reflected in the drugs' label which carries a warning related to treatment emergent hyperglycemia and diabetes mellitus.

The study enrolled 48 healthy pre-menopausal women, randomizing them into two arms: Subjects in the treatment arm (24 women) were administered 144 mg/day Histalean™ and subjects in the control arm were administered matching placebo. One week later, all of the subjects started treatment with Olanzapine, and co-administration of Olanzapine with either Histalean™ or matching placebo continued for an additional three weeks. Subjects were monitored regularly throughout the study period for vital signs, adverse events (AEs), blood tests and urinalysis, in order to assess safety parameters.

Preliminary safety analysis was positive. No serious adverse events (SAEs) were recorded, with about 95% of the subjects completing the entire treatment period. Adverse events were mild to moderate and most were characteristic of Olanzapine. Furthermore, no statistically

significant differences were found in any of the functional safety and lab parameters between the treatment arm and the control (placebo) arm. This outcome validates the benign safety profile of Histalean™, even when administered at a three-fold the standard dose and in combination with an antipsychotic drug.

In parallel with the safety analysis and in order to explore the capacity of Histalean™ to mitigate weight gain associated with the Olanzapine, Obecure conducted a statistical analysis to evaluate the weight changes over time in the study subjects in the intent-to-treat (ITT) population (N=46). As expected, Olanzapine resulted in significant weight gain in both study arms. However, the mean weight gain of subjects in the Histalean™ arm (1.2 Kg) was substantially (37%) and statistically significantly lower than the mean weight gain of subjects in the placebo arm (1.9 Kg;  $p < 0.05$ ). Moreover, a categorical statistical analysis of the proportion of subjects that gained more than 2 Kg indicated a statistically significant difference favoring the Histalean™ treatment group: 52% of the subjects treated with the placebo/Olanzapine combination gained  $> 2$  Kg, as compared to only 23% of the subjects on the Histalean™/Olanzapine combination ( $p < 0.05$ ). This analysis has important clinical implications as it reflects a reduced risk of metabolic complications in subjects co-treated with Olanzapine and Histalean™. This outcome is impressive, considering the small number of subjects (24 or 22 in the treatment and placebo arms, respectively) and the short treatment duration in this POC study.

Dr. Nir Barak, M.D., the inventor and CSO of Obecure explained that "the idea of combining Histalean™ with antipsychotic drugs to mitigate their associated weight gain was based on an analysis of their respective potential mechanisms of action. Histalean™ is a histamine mimetic and activates the H1 receptor in the brain. Olanzapine and many of the other atypical antipsychotic drugs act by modulating the activity of neurological receptors, most importantly those involved in dopaminergic and serotonergic signaling; Inadvertently, they also inhibit the same H1 receptor that binds Histalean™. It has been suggested that this receptor inhibition is responsible for the weight gain side effect. The hypothesis tested in this study was: would Histalean™ be able to offset the H1 inhibitory effect of Olanzapine and thus attenuate the weight gain? The answer to this according to the study results seems to be – Yes".

"The Company is currently assessing its path forward and evaluating alternative strategic possibilities such as partnering for further development and commercialization and/or attracting investments in order to conduct more advanced Phase II/III independently." said Dr. Ami Eyal, CEO of Bio-Light, adding that "the commercial opportunity of a "safer" combination drug is obvious, considering the annual turnover of \$12 billion in this market which faces imminent patent expiries.

Obecure is also developing Histalean™ for obesity and is currently awaiting results of its recently completed Phase IIb clinical trial in obese premenopausal women, which was conducted in Germany, Belgium and the Netherlands.

## **About Obecure**

Founded by Biolight in 2005, Obecure is focused on the development of weight management drug therapies, based on clinical evidence showing that betahistine (active drug in Histalean™) is effective in reducing weight in obese women. Obecure has a worldwide exclusive license from Mor Research Applications Ltd., the Technology Transfer Office of Clalit HMO to clinically develop and commercially exploit the technology, as developed by Dr. Nir Barak, a specialist in internal medicine and clinical nutrition.

The Company is currently pursuing the clinical development of its lead compound Histalean™ for general obesity and for weight gain associated with anti-psychotic drug therapy.

For more information: [www.obecure.com](http://www.obecure.com)

## **About Histalean™**

Histalean™ is comprised of betahistine, approved and marketed worldwide, except in the United States, for the treatment of Meniere's disease (vertigo). Betahistine is an H1 receptor agonist and partial H3 receptor antagonist. It has an excellent safety profile established over >40 years of treatment by more than 100 million patients suffering from vertigo and dizziness. This safety is of great advantage when compared to other weight management drugs which are approved or are in development.

## **About Bio- Light**

Bio-Light Israel Life Science Investments Ltd. is a holding company traded publicly on the Tel Aviv Stock Exchange (TASE:BOLT). Bio-Light specializes in life science technology development and currently operates a group of three subsidiary companies: Obecure, IOptima and Zetiq.

Bio-Light was founded in 2005 by a group of professionals highly experienced in all aspects of the Israeli life science investment environment. This team provides the Bio-Light subsidiaries with ongoing support, resources and expertise in science, regulation, business development, and intellectual property.

For more information: [www.bio-light.co.il](http://www.bio-light.co.il)

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