"The Pink Sheet"
DAILY

OCTOBER 28, 2015

BioBlast Skips To Phase III In Rare Form Of Muscular Dystrophy

Biotech plans Phase III program for I.V. sugar formulation Cabaletta in oculopharyngeal muscular dystrophy, after reporting limited, proof-of-concept data for the rare, debilitating swallowing disorder.

Israeli biotech **BioBlast Pharma Ltd.** is headed toward a Phase III study of its Cabaletta in a rare, muscle-wasting disease that causes problems with swallowing, after reporting positive results from a Phase II trial stopped early based on positive signs of efficacy.

The company is developing Cabaletta (I.V. trehalose) as a once-weekly drug for oculopharyngeal muscular dystrophy, an inherited disorder that is debilitating and can prove fatal.

Trehalose is a naturally occurring sugar used in the food and pharma industry as a protein stabilizer. BioBlast says it has strong methods of use patents for its Cabaletta formulation.

In the US, no drug is approved for OPMD and Cabaletta has orphan drug status and fast track status for this indication.

In an Oct. 27 investor call, the company presented interim data for 25 patients enrolled in the open label Phase II HOPEMD study, which compared Cabaletta's effects relative to patients' own baseline levels, providing a proof-of-concept for the program.

The company will be talking to FDA late this year or early next year regarding starting a Phase III study in 2016, likely using similar endpoints. BioBlast expects that the study will be a double-blind, randomized controlled trial of 80 patients in six US centers and three Canadian facilities. The plan is to study patients for nine months, followed by a three-month continuation phase.

OPMD primarily affects people living in the southwest of the US, French Canada and Israel. From 4,000 to 6,000 have it in the US, according to the company (*see box*).

The condition causes trouble swallowing (dysphagia), drooping of eyelids and muscle weakening in the lower and upper body. The dysphagia is the worst problem because patients can't eat, resulting in aspiration of food, dehydration and emaciation.

The original goal with HOPEMD, which was conducted in Israel and Canada, was to evaluate about 70 people with moderate cases of OPMD. Patients would be treated for 24 weeks, then randomized to treatment vs. non-treatment arms. However, the company wound up stopping the study prior to randomization, due to signs of efficacy, and decided to move immediately to a later-stage trial. The patient population is small and it would have been unethical to continue, BioBlast explained.

Its interim analysis reflects data available as of Sept. 1 for 25 people in the study, as compared to the patients' own baseline levels, including 22 who were treated for six months.

The company reported dysphagia data for 12 evaluable patients in the study. Ten of those 12, or 83.3%, stabilized or had numerical improvement in symptoms of dysphagia, assessed with the Penetration Aspiration Scale using video fluoroscopy, an eight-point scale that assesses ability to swallow. Of the 12 evaluable patients, half improved numerically on this measure as opposed to merely stabilizing. Baseline images for other patients were not sufficient for assessment, the company said.

Stabilizing disease is a good outcome for these patients, given disease severity and the typical rate of decline, let alone improving disease, CEO Colin Foster suggested during the call. So, improvement was an "unexpected finding in this relentlessly progressive disease."

"We believe this is the first time a pharmaceutical intervention has shown potential evidence of clinical evidence

How Common Is OPMD?

- 1-9 per 100,000
- 4,000 to 6,000 in US
- 1 per 1,000 in French Canadians/Quebec
- 1 per 100,000 in EU
- 1 per 700 Bukhara Jews in Israel

in OPMD with the possibility of actually improving various clinical aspects of the disease," Foster said.

There was a statistically significant improvement of 35.3% compared to baseline in the timed cold water drinking test, another important measure used to screen patients for dysphagia, in 20 patients in the study. There were signs that some patients respond quickly, as 4.2% benefited after just one week of therapy, though this was not a statistically significant result.

And results for 21 patients responding to a quality of life symptom score suggested a statistically significant improvement of 12.1%, which the company says illustrates that the drug's effects are clinically meaningful.

The company saw a statistically significant improvement in a number of other endpoints, as well as numerical improvements in some other measures. For example, there were statistically significant improvements in most of the lower-extremity muscle function scores, and positive trends in upper extremities.

"The totality of the data gives us confidence that a proof-of-concept for Cabaletta in OPMD patients has been demonstrated in this study," Chief Development Officer Dalia Megiddo said.

No notable differences in efficacy between types of patients were observed in the trial, execs said during the call.

No change in weight was observed compared to baseline in the trial, and Cabaletta was safe and well-tolerated, with no drug-related serious adverse events, the company reported.

The HOPEMD study involved a six-month period of treatment and follow-up for 12 months. A full set of data will read out at the end of 2016.

In addition to OPMD, Cabaletta is also in Phase II development for the genetic neurodegenerative disorder Spinocerebellar Ataxia Type 3 (SCA3) CA3, or Machado Joseph disease.

By Emily Hayes