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Longboard Surfs PACIFIC Waves To Pivotal Phase III Epilepsy Program

by Alaric DeArment

The company's valuation quadrupled after it announced positive Phase Ib/IIa results for bexicaserin in Dravet syndrome, Lennox-Gastaut syndrome and other epileptic disorders.

Longboard Pharmaceuticals, Inc.'s management offered some tidbits about its plans for a Phase III trial program of bexicaserin after the announcement of positive data from the Phase Ib/IIa PACIFIC trial in patients with developmental and epileptic encephalopathies (DEEs), even as it kept many details of its Phase III plans, including timelines, close to its chest.

The La Jolla, CA-based company announced the results of PACIFIC on 2 January, in patients with Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS) and other DEEs. Chief medical officer Randall Kaye told a same-day call with analysts that the company plans to have an end of Phase II meeting with the US Food and Drug Administration, which would be part of the Phase III planning, but the company is still uncertain about the timing.

Shares of Longboard closed at $25.10, up 316.3% from the company's 29 December 2023 closing price of $6.03.

Fair Winds On The PACIFIC

The Phase Ib/IIa PACIFIC study enrolled 52 participants aged 12-65 across 34 sites in the US and Australia who had DS, LGS or another qualifying DEE – classified as "DEE Other" – and who received bexicaserin at 6mg, 9mg and 12mg three times per day or placebo. Of the 52 participants, 43 received bexicaserin, also known as LP352, including four with DS,

Key Takeaways

- Longboard Pharmaceuticals announced positive results of its Phase Ib/IIa PACIFIC trial of bexicaserin in patients with epileptic disorders.

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24 with LGS and 15 with other DEEs. Among the nine patients in the placebo group, none had DS, while five had LGS and four had another DEE. Patients were allowed to take up to four standard anti-seizure medications, with the most common being *Jazz Pharmaceuticals plc*'s Epidiolex (cannabidiol), *Assertio Holdings, Inc.*'s Sympaza (clobazam) and the generically available lamotrigine levetiracetam.

- In response to the results, the company's share price quadrupled, closing up more than 300% from its closing price on the last trading day of 2023.
- The company is planning a pivotal Phase III trial program for the drug and provided some details of its plans in a call with analysts.

According to the PACIFIC results, the median change in countable motor seizure frequency – the trial's primary efficacy endpoint – was a 53.3% decrease from baseline among patients receiving bexicaserin, compared with 20.8% for the placebo arm. The median change in the individual cohorts was 72.1% for DS, 48.1% for LGS and 61.2% for other DEEs.

"These results were demonstrated on top of contemporary polytherapy background, so this is essentially a real-world experiment that helps us understand that you can take patients that are on a variety of additional [anti-seizure medications], provide another medication and have incremental clinically meaningful important incremental benefit above and beyond," Kaye told the analyst call.

In terms of safety, nine participants in the bexicaserin group discontinued treatment due to an adverse event, including two during the maintenance period and seven during the titration period. No patients in the placebo group discontinued treatment, and there were no deaths reported in the study. Three patients, all in the bexicaserin arm, reported a serious adverse event, namely ankle fracture, constipation and increased seizures.

"The results were highly positive, showing that bexicaserin achieved a median reduction of approximately ~53% in countable motor seizures, meaningfully outperforming the placebo group's ~21% across a diverse range of DEEs," B. Riley Securities analyst Kalpit Patel said in a 2 January note.

Evercore ISI analyst Gavin Clark-Gartner said the results indicated bexicaserin is "at least as efficacious" as *UCB S.A.*'s DS and LGS drug, Fintepla (fenfluramine).

"This is within the best-case scenario for the readout. [The] only way the efficacy could've looked much better would have been lower variability/outliers across both arms," he said.

Phase III Plans

Longboard is planning a global Phase III program, which CEO Kevin Lind told the call would be "a Phase III program, not just individual clinical studies," adding that the company would design the program to achieve multiple goals, namely "time to market, broad usage, and commercially and clinically relevant differentiation."

In addition, Lind said the company is planning to use twice-daily dosing for the Phase III program and that "there is some potential IP that could be generated around dosing."

Longboard is also looking at multiple paths for how to structure the Phase III program, with Lind saying that one possibility is going with three simultaneous, individual Phase III DEE programs – e.g. one for DS, one for LGS and one for a third indication, which he called "very consistent with what everyone else has done." Still, time to market is an important consideration, he said.

"So, there is a chance that as part of that Phase III program, if we go down that path of going after the broad DEE approach rather than each one sequentially, we could pull out one or two of those and think about a faster time to the market," he said. "If we do the broad DEE approach, our thought is, it is not the PACIFIC study just grossed up and super-sized – it will have some creative bells and whistles built in along the way and hedges that we are not ready to disclose today as we continue to look at the data set, but I think it is entirely likely that we could think through some creative ways to get there faster."