Evaluate Vantage

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End of an era for Tetraphase

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The world needs new antibiotics, but after its wholesale phase III failure Tetraphase Pharmaceuticals' eravacycline is unlikely to become one. The miss in the Ignite 2 urinary infection trial might not have done for the project – an approval trial in abdominal infection hit when it reported in December – but the antibiotic's future, and that of the company, is far from clear.

Tetraphase made much of an Ignite 2 subgroup analysis showing that eravacycline beat its comparator, levofloxacin, in a subset of patients with quinolone-resistant bugs. But that was not enough for its shareholders, who wiped 79% off the group's value thanks to the overall trial results.

The new data are from the second, pivotal, part of the Ignite 2 study – the first was designed to identify the dose to be used for the approval phase. It saw 908 patients with complicated urinary tract infections randomly assigned to receive eravacycline or the generic drug levofloxacin, in both cases with an initial IV dose followed by oral administration.

Each patient received a minimum of three days of IV dosing – eravacycline 1.5mg/kg or levofloxacin 750mg, each every 12 hours – and then, if clinically indicated, oral therapy to bring the total treatment period to seven days. The oral doses were 200mg orally every 12 hours for Tetraphase's project and 750mg every 24 hours for levofloxacin.

The Ignite 2 data were to support both US and European approval, using different endpoints. For the FDA, this was a combination of clinical cure rate and microbiological response 6-8 days after the completion of therapy. For the EMA, the primary endpoint was microbiological response in a slightly different population at the same time point.

For both a 10% non-inferiority margin was used. Nevertheless eravacycline missed.

The way forward

The path from here is unclear; on a conference call Tetraphase said it had not yet talked to the FDA about what more could be done, and would not say when a deeper analysis of the data might emerge.

The company ended its second quarter with $242m in cash, enough to sustain it until 2017, but with no other late-stage projects its fortunes remain tied to eravacycline. Perhaps approval in abdominal infections might be granted based on the Ignite 1 data.

It has previously said that the two trials together would form the basis of regulatory submissions for eravacycline in both indications, but it is not clear whether one on its own would be sufficient for a more limited approval.

If the company is determined to pursue the UTI indication, studying the project in quinolone-resistant patients is a possible way forward, based on the pre-specified subgroup analysis. But again this will take time and money, and Tetraphase has plenty of cash to string out the process rather than throw in the towel.

The company's chief executive, Guy Macdonald, can congratulate himself on avoiding some of the fallout, having sold 10,000 shares last week at $41.57 apiece. At time of press the stock was trading at $9.40.

Study	Trial ID
Ignite 1	NCT01844856
Ignite 2	NCT01978938

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