Evaluate Vantage

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Event - Cypress seeking pain relief with milnacipran approval

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Cypress Bioscience, a classic one-product biotech, is entering a defining period with a PDUFA due in late October over its new fibromyalgia syndrome (FMS) treatment, milnacipran, presenting potential investors with a prime example of a high-risk high-return investment dilemma.

With Cypress's shares falling 63% over the last 12 months to $5.61, trading just above cash levels of $4 per share, investors have clearly decided the risk outweighs the potential returns. However, as the drug is potentially worth $478m or $12.58 per share, according to EvaluatePharma's NPV Analyzer, should the FDA approve milnacipran the upside is significant.

Delay on safety concerns

Milnacipran is an SNRI anti-depressant, discovered by Pierre Fabre and marketed in Europe since 1997. Cypress licensed North American rights to the drug in 2001 and subsequently contracted Forest Laboratories in 2004 to takeover responsibility for phase III trials and commercialisation.

Despite milnacipran's 11-year marketing track record in Europe, many are concerned that safety issues such as a potential to raise blood pressure will cause the increasingly safety-conscious FDA to seek a delay of up to six months, in order to review the results of a specific ambulatory blood pressure trial, due by the end of the year.

Others fear that in spite of having accepted Cypress's NDA containing data from the first two phase III trials and not suggesting any further information will be required, the FDA could ask to review the safety and efficacy data from a third phase III trial, also due by year-end.

As such, the consensus among analysts appears to expect a delay to approval, whilst acknowledging that the drug's efficacy means it should be approvable, suggesting the FDA may issue one of its newly-termed complete response letters.

Potential blockbuster

Whilst claims by some analysts that milnacipran has blockbuster potential is probably on the blue-sky end of estimates, consensus forecasts for sales by Forest of $690m by 2014 indicates the size of the opportunity.

With Cypress to receive royalties of around 15%-20%, analysts have pencilled in revenues of $20m in 2009 growing to $118m by 2014. On the basis that the FDA approves milnacipran without significant delay, prompting a significant milestone payment, Cypress may become a rare breed within small biotech circles by recording a net profit as soon as next year.

However, an FDA approval is unlikely to be the only battle the product faces if it is to be a big commercial success. The drug's composition of matter patent expired in 2002 meaning it will only be protected beyond the expiry of NCE exclusivity in 2013 or 2014 - depending on when the drug is approved - by generally weaker method-of-use patents to 2021.

Therefore, it could be a victim of its own success if sales meet expectations, making it an attractive target for an aggressive patent challenge from the big generic companies.

New treatments welcome

FMS is a chronic condition characterised by pain and stiffness throughout the body, accompanied by severe fatigue, insomnia and mood symptoms. But unlike other rheumatological disorders it is not caused by inflammation, thought instead to be down to abnormal pain processing within the central nervous system, commonly triggered by physical trauma, emotional stress or infection.

Despite affecting 2%-4% of the US population, or four to six million patients, Pfizer's anti-epileptic drug Lyrica

was the first drug to be officially approved to treat FMS in June last year. Coupled with the recent approval of Eli Lilly’s anti-depressant Cymbalta for FMS, the field is suddenly increasingly competitive, although analysts believe a new treatment for FMS will help to grow the size of the market opportunity rather than cause intense competition.