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Roche picks up pace on ImmunoGen antibody drug conjugate

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It may be more than three years before researchers report phase III data on the antibody drug conjugate T-DM1 in HER2-positive metastatic breast cancer, but that is not stopping Roche from applying for marketing authorisation on the back of phase II data. In its quarterly earnings release, the Swiss company announced that after discussions with the FDA it will be submitting an application in 2010 for the combination of Herceptin and ImmunoGen's targeted chemotherapy agent DM1.

Shares in ImmunoGen rose 2% to $9.40 in early trading today following Roche's announcement, an indication that investors were already expecting an accelerated filing for T-DM1 this year. With analysts setting price targets for ImmunoGen between $9.50 and $14, it appears expectations are high that the candidate will be approved and eventually yield the $135m in royalties in 2016 forecast by *EvaluatePharma's*consensus of analysts.

Shrinking tumours

Phase II data reported late last year indicated that T-DM1, known generically as trastuzumab emtansine, reduced the size of tumours in 33% of the 110 patients enrolled, and in 45% produced a clinical benefit, such as tumour response or stable disease maintained for at least six months. It also resulted in fatigue in 59%, nausea in 37%, and thrombocytopenia in 5.5% of patients (*Seattle deal and ImmunoGen data mark growing interest in conjugate field, December 17, 2009*).

To qualify for that study, patients had to have failed on at least two HER2 targeted treatments in the metastatic setting, an anthracycline, a taxane and Xeloda; essentially patients with no options left to try.

Whilst it is unusual for a company to submit an application on the basis of phase II data, it is not unprecedented in very sick populations; Allos Therapeutics' Folotyn gained approval last year for T-cell lymphoma on the basis of phase II data alone. More robust data is more than three years away, from a 580-patient pivotal trial pitting T-DM1 against Xeloda plus Tykerb in patients who have failed on a taxane and Herceptin.

As such, a surrogate marker like tumour shrinkage, instead of survival data normally required, may be adequate to support conditional approval in this population of very sick patients.

Speaking to *EP Vantage*today Daniel Junius, chief executive of ImmunoGen, noted that there are numerous trials for T-DM1 that will add "depth" to safety data for purposes of an FDA submission.

Long road

ImmunoGen licensed the pre-clinical T-DM1 to Genentech, now a part of Roche, in 2000 in a worldwide deal for $2m upfront and up to $44m in regulatory and development milestones. So far, $13.5m have been paid out.

Mr Junius said ImmunoGen will not receive another milestone for T-DM1 in this specific indication until approval, should it come, and it will be "something less than half" of the money still available as part of the license. Additional trials are under way for first-line and combination treatment in metastatic breast cancer under its license with Roche.

The company ended 2009 with $51.2m, and Mr. Junius expects to have more than $30m remaining at the end of its fiscal year, on June 30. He estimated that would be a year's worth of cash without licensing its two unpartnered pipeline assets, lorvotuzumab mertansine (IMGN901) and IMGN388, on which Johnson & Johnson has opt-in rights in a co-development deal.

As its entire pipeline with the exception of T-DM1 remains in phase I trials, the Roche-partnered drug remains the group's most valuable asset and as such, it will be on this candidate that the company and its investors remain focused.

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