Mustang Bio sets its sights on 2021 approval

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Its gene therapy is three years away from market, but Mustang is already thinking about outcomes-based pricing.

The publication of promising clinical data on MB-107, Mustang Bio's gene therapy for X-linked severe combined immunodeficiency, caused a great deal of excitement last month. It will be crucial that expectations for this project are borne out by more evidence from its current clinical trials if it is to make a mark in this rare disease.

“We do think that it’s very realistic to file for newborns at the end of 2021, with approval in the middle of 2022,” Manny Litchman, chief executive of Mustang, tells Vantage. And at a time when the cost of these products is prompting a great deal of concern, Mustang is already thinking about a pricing model where it would only receive payment for successful treatment.

The X-SCID data so far are positive – but the key phrase is “so far”. Last month the company reported data on the first eight infants in a trial that will go on to enrol 28 patients aged two months to two years. This is a decent start, but much remains to be proven (Mustang and the bubble boy bubble, April 18, 2019).

At least the company knows its path ahead – because it intends to follow in the footsteps of the only company that has so far obtained approval for an immunodeficiency gene therapy. Orchard Therapeutics’ Strimvelis was approved for a different form of the disease, SCID due to adenosine deaminase deficiency, in Europe in 2016.

But it is Orchard’s other lentiviral gene therapy for ADA-SCID, OTL-101, that provides Mustang with a clinical and regulatory template.

“We do think of Orchard as a model,” says Mr Litchman. “A different disease, a different gene therapy, but nevertheless a very similar regulatory approach.”

Next steps

The next steps, according to this blueprint, will be to compare the data with the ten patients that have been treated with MB-107 – two of them subsequent to last month’s data cut – with retrospective historical controls in healthcare databases. It will be crucial to show improvements in event-free and overall survival, Mr Litchman says, as well as endpoints including freedom from infection and mutagenesis.

Every patient treated with any gene therapy has to be followed for 15 years to assess issues around mutagenesis, leukaemogenesis and long-term side effects, but two-year data will be sufficient for submission
to the FDA.

A parallel trial is also ongoing in patients who have failed after previous treatment with stem cell transplant. Mr Litchman says this population represents a much larger reservoir of patients than newly-diagnosed infants, at “several hundreds in the US and quite a bit more outside the US”. This compares with an incidence of X-SCID in the US of only about 20 patients a year, he says.

Mustang estimates that the next release of MB-107 data will come in the second quarter of 2020, and hopes it may be able to file the BLA for previously treated patients at the same time it files for newborns – by the end of 2021. But it is possible that the previously treated patients will be the subject of a supplemental BLA which will follow later, Mr Litchman says.

**Pricing**

If clinical and regulatory pitfalls are negotiated successfully, an even bigger challenge awaits: pricing.

“We watched very carefully as Bluebird launched its Lentiglobin in Europe and talked about pricing in the $2m range, but with a reimbursement model where payers could pay for success,” Mr Litchman says.

“We would be happy to endorse a model where patients or payers could pay out over a relatively long period of time – even 10 years. Then if the therapy stopped working the payers would stop paying.”

Its investors are not fazed by the prospect of waiting so long for a payday, Mr Litchman says, partly because a steady source of slow-burn income is appealing to some. The other reason investors are sanguine is that the company also has a raft of CAR-T products in the clinic which could also be lucrative.

The most recent development in its CAR-T franchise is the initiation last week of a phase I multiple myeloma trial for MB-104, which targets the CS1 protein rather than the BCMA antigen which is more commonly targeted, including by Bluebird Bio’s Lentiglobin. Mr Litchman says that at least three patients will be treated in the trial by the end of the year.

Another pipeline hope, MB-102, is directed against the CD-123 antigen and is in phase I trials in patients with blastic plasmacytoid dendritic cell neoplasms. Again the company has a forerunner of a sort: Mr Litchman says that most people had never heard of this disease until Stemline’s CD123-directed fusion toxin, now called Elzonris, got approval in December of last year.

MB-102 is also in trials in AML, in which two out of five patients have reached minimal residual disease-negative status at the 200 million cell dose level, and one out of two complete responders at a dose of 100 million cells for BPDCN. Further data from these trial are expected towards the end of the year.

Other CAR-Ts are in clinical trials in glioblastoma and non-Hodgkin’s lymphoma, and studies are planned in prostate and pancreatic cancers.

Funding for all these studies will be partly provided by the $30m fundraising the group did late last month. But more money will be necessary to see all these pipeline projects to market, and no investors are patient forever. Mustang must hope that MB-107’s efficacy holds up long-term, so that the money keeps trickling in.