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Mesoblast Falls 58% On 2nd US FDA CRL For Remestemcel-L For GvHD

Mesoblast fell as much as 58.3 percent following the US Food and Drug Administration's second refusal of injected remestemcel-L for paediatric graft versus host disease.

Mesoblast said the FDA had provided a complete response letter (CRL) to its biologics licence application (BLA) resubmission for remestemcel-L, or Ryoncil, for paediatric steroid-refractory acute graft versus host disease (SR-aGvHD).

The company said the FDA "requires more data to support marketing approval".

In 2020, Mesoblast said the FDA required a further trial of Remestemcel-L for graft versus host disease and "recommended that [it] conduct at least one additional randomized, controlled study in adults and/or children to provide further evidence of the effectiveness of remestemcel-L for … graft versus host disease" (BD: Oct 2, 2020).

Today, a conference caller said the additional trial was not required, and the company said that "to obtain the data required … [it would] conduct a targeted, controlled study in the highest-risk adults with the greatest mortality".

Mesoblast said the adult study was "in line with our overall commercial strategy, which envisioned a sequenced progression from paediatric to adult SR-aGvHD indications".

The company said that adults comprised 80 percent of the SR-aGvHD market.

In the media release, Mesoblast chief executive Prof Silviu Itescu said: "FDA's inspection of our manufacturing process resulted in no observed concerns, the Agency raised no safety issues across more than 1,300 patients who have received remestemcel-L to date, and acknowledged improvements to our potency assay."

“We remain steadfast in making remestemcel-L available to both children and adults suffering from this devastating disease and have received substantial clarity in how to bring this much-needed product to these patients,” Prof Itescu said.

The company said it intended to enrol adult patients at the highest mortality risk with SR-aGvHD where existing therapy had not improved outcomes, and 90-day survival was as low as 20 percent to 30 percent.

Mesoblast said it generated pilot data through its emergency investigational new drug application program in adults showing a survival benefit with remestemcel-L.

The company said that “in-line with our overall commercial strategy to expand into the adult SR-aGvHD indication” it had been working to establish the adult follow-on study protocol, potentially utilizing established clinical trials networks and it would “seek alignment with FDA on the trial design … within 45 days”.

The company said prior to the resubmission, the FDA guided Mesoblast to resolve outstanding chemistry, manufacturing and controls issues before any additional trial.

Mesoblast said the FDA completed the pre-licence inspection of the manufacturing facility, did not issue any Form 483, and found no objectionable conditions, and acknowledged in the resubmission review that changes implemented appeared to improve assay performance relative to the original assay version used in the paediatric phase III trial.

Mesoblast said it met the pre-specified primary endpoint, prospectively agreed with the FDA, of a single-arm phase 3 trial in 54 children with SR-aGvHD.

The company said the resubmission included long-term follow-up data from the phase III trial by the Center for International Blood and Marrow Transplant Research showing 50 percent survival through more than four years of follow-up for remestemcel-L treated patients for whom less than 20 percent survival at two years was expected based on disease severity.

Mesoblast said the resubmission included a post-hoc, propensity-matched study showing six-month survival was 67 percent with remestemcel-L compared to 10 percent with other unapproved therapies in highest-risk patients.

Mesoblast closed down 62 cents or 56.9 percent at 47 cents with 89.8 million shares traded.