Evaluate Vantage

November 29, 2021

Krystal shines in epidermolysis bullosa

Madeleine Armstrong

Look out Amryt: Krystal's topical gene therapy is gaining ground.

There are currently no approved therapies for the rare skin disorder epidermolysis bullosa, but two might soon hit the market in quick succession. Krystal Biotech today reported impressive top-line results from the pivotal Gem-3 trial of its topical gene therapy Vyjuvek, setting up a filing in the first half of next year.

The news comes not long after Amryt announced a three-month delay to the FDA's review of its project, Filsuvez, to February 28, 2022. Two other EB gene therapies, from Abeona and Castle Creek, are due to yield pivotal data next year, so competition could get fiercer yet.

Gem-3

For now, this will not trouble Krystal, whose shares rocketed 130% this morning. Gem-3 met both its primary and secondary endpoints – complete wound healing at six and three months, respectively.

The trial enrolled 31 patients with dystrophic EB, which is caused by mutations in the *COL7A1* gene. Vyjuvek, formerly known as B-Vec, is designed to deliver this gene via an attenuated herpes simplex viral vector.

In Gem-3, two primary wounds were selected for each patient that were similar in terms of size, location and the time they had been open wounds. One wound was treated with Vyjuvek while the other received placebo, meaning patients effectively acted as their own controls.

Patients received once-weekly treatment until their wounds closed. If the wound reopened, treatment resumed – one potential advantage of Vyjuvek is that it can be redosed.

At six months, 67% of Vyjuvek-treated wounds were completely healed, versus 22% of placebo-treated wounds. At three months, the figures were 71% and 20% respectively.

This indicates that some wounds that had closed at three months subsequently reopened, something that can happen in the course of EB, and which has been seen before with Krystal's gene therapy (*Gene therapy's duration is less than Krystal clear, October 29, 2019*).

During a conference call today Krystal execs were reluctant to say more on the project's durability, though this should become clearer when the company reports more data at a scientific meeting next year.

Another question is how Vyjuvek performed in recurring versus chronic wounds – in a much smaller phase 2 trial, the project worked better in the former. Again, more details should emerge with the full data, but the lead

investigator of Gem-3, Dr Peter Marinkovich of Stanford University School of Medicine, noted that the study encompassed both wound types.

Home dosing?

In Gem-3, Vyjuvek was administered in the clinic, but Krystal also believes that home treatment could be possible. The group hopes to start home dosing in its open-label extension trial in the first quarter of next year.

It is not clear whether any approval could initially cover home dosing, but Krystal's chief commercial officer, Andy Orth, said the group will be "prepared for every eventuality". However, he does not expect home dosing to represent the main setting for therapy if Vyjuvek is approved.

In any case, Vyjuvek looks much more convenient than the other EB gene therapies in development, which involve surgical transplantation and intradermal injections (*Epidermolysis bullosa gene therapies wait in the wings, April 28, 2021*).

Amryt's Filsuvez (Oleogel-S10), a topical gel formulation of the plant extract betulin, represents another patient-friendly option. However, this project's phase 3 trial, Ease, in dystrophic and junctional EB, was far from a slam-dunk: it met its primary endpoint, wound closure at day 45, but fell short on the key secondary, wound closure at day 90.

Sellside consensus from *Evaluate Pharma* puts 2026 sales of Vyjuvek and Filsuvez at $462m and $269m respectively.