Bluebird exits Europe as another hold hits

The business split is still on, but problems mount for the genetic disease wing of Bluebird.

Bluebird Bio only recently resolved the clinical hold for Lentiglobin. Now it has been hit with another safety scare, this time with its other lentiviral vector-based gene therapy, Lenti-D. The company was quick to dismiss fears of a read-across to Lentiglobin, but similarities between the holds could give investors pause.

And that was not the only bad news dropped today during the group’s second-quarter earnings: Bluebird confirmed plans to wind down its operations in Europe after failing to strike deals with payers there. The company is still on track to split into separate gene therapy and oncology businesses in the fourth quarter, but the rationale for doing so now looks even shakier than before.

Bluebird opened down 23% today, and its market cap now sits at $1.3bn, not far off cash.

Second hold

Bluebird’s previous hold, for Lentiglobin, came after two cases of cancer – acute myeloid leukaemia and myelodysplastic syndrome – were reported in the project’s sickle cell disease trial (Bluebird split looks premature, February 16, 2021).

The group later ruled out its lentiviral vector as the cause of the AML, and concluded that the case of MDS was, in fact, transfusion-dependent anaemia. The hold was lifted in June.

The latest hold came after a patient developed MDS around a year after being treated with Lenti-D in the phase 3 ALD-104 study in cerebral adrenoleukodystrophy (CALD). This time, Bluebird has already concluded that the case was likely mediated by the lentiviral vector used in Lenti-D.

But the group still hopes to gain approval of Lenti-D based on the current dataset, saying the risk/benefit profile of the project remains favourable given the “devastating consequences” of CALD and the shortcomings of the current standard of care, allogeneic stem cell transplant.

Bluebird plans to complete its rolling BLA by the end of 2021. Lenti-D recently got the go-ahead in Europe, where it is branded Skysona, although presumably the group will not be selling it there given today’s announcement.

Expectations are low for Lenti-D, with the sellside only forecasting $97m sales by 2026, according to Evaluate Pharma’s consensus. Around a quarter of these sales had been expected to come in Europe.
No readthrough?

The bigger prospect at present is Lentiglobin, which is expected to bring in $723m the same year – although this figure has fallen from $1.5bn before Bluebird’s first clinical hold. The gene therapy is branded Zynteglo in Europe, where it has long had a hard time gaining reimbursement, so perhaps Bluebird’s move to exit the continent is not entirely surprising.

The company believes that Lentiglobin still has a future in the US and is adamant that the latest hold has no implications for that gene therapy. During today’s second-quarter call executives pointed out the differences between the two therapies: Lenti-D employs a promoter call MNDU3, which leads to broad tissue expression and high levels of expression across all cell types, while Lentiglobin uses the BB305 vector, designed for specific expression only in cells that could become red blood cells.

Bluebird added that no other lentiviral vector haematopoietic stem cell gene therapies used the MNDU3 promoter, something that should be good news for others in the space.

Still, the latest news will only increase nervousness around the use of lentiviral vector-based gene therapies, which will be the lynchpin of Bluebird’s business once its oncology arm is spun off to become 2seventy bio.

Perhaps Bluebird would be better off cutting its losses in rare diseases and focusing on cancer, without the distraction of a spin-off.