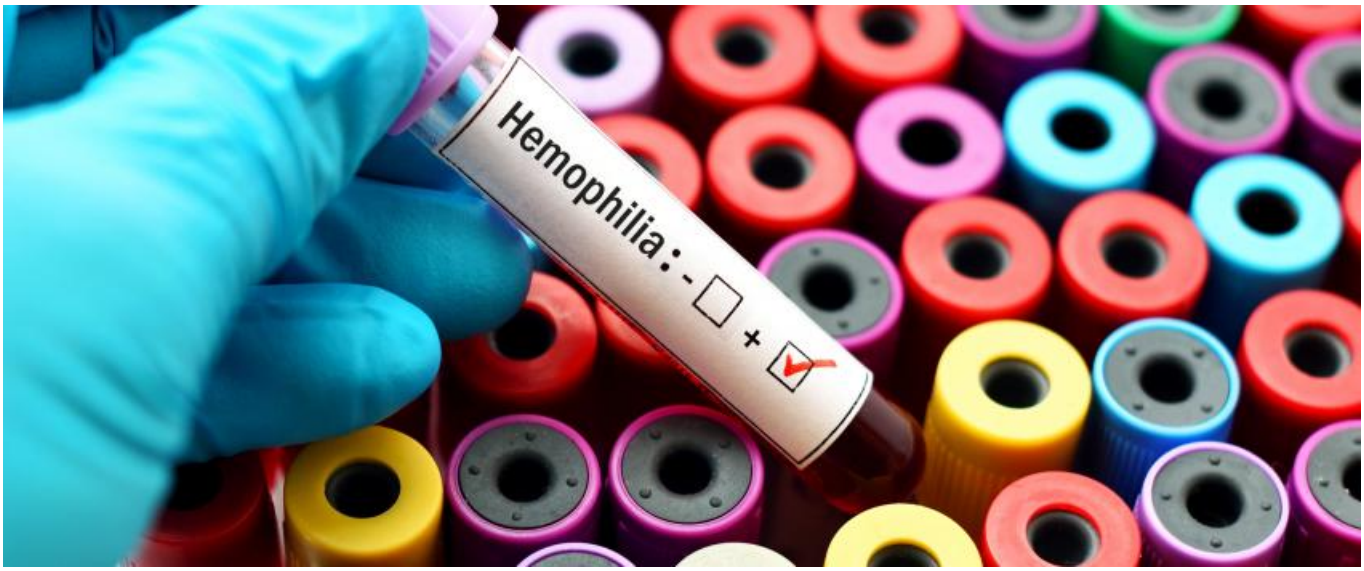
Evaluate Vantage

June 25, 2020

No buyout for Uniqure

Jacob Plieth



But a licensing deal with CSL could have underappreciated benefits, even if expectations were for something much bigger.

The problem with being a top biotech takeout pick is that when instead of getting taken over you do a licensing deal the market comes down on you like a ton of bricks. Arcus found this out in May, and yesterday is was Uniqure's turn.

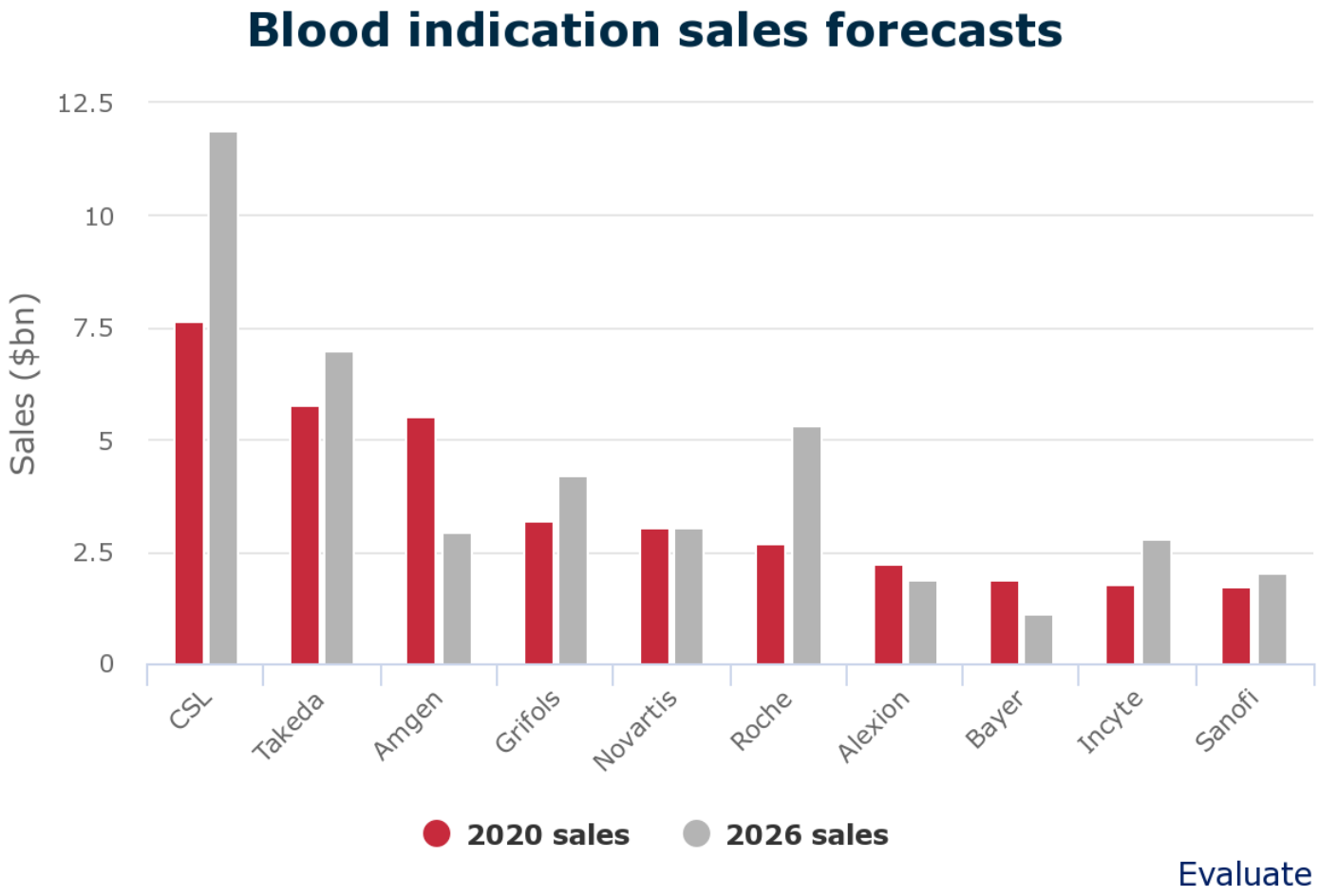
The partner Uniqure has chosen for its haemophilia B gene therapy – not a major pharma company but Australia's CSL – might have resulted in a double-whammy of investor disappointment; Uniqure opened off 18% today. Still, the might of CSL in blood disorders should not be underestimated, though the deal is quite backend-loaded.

Even so, the $450m up-front fee is impressive considering that the gene therapy in question, etranacogene dezaparvovec, has only generated data in three subjects. Uniqure will continue running the pivotal Hope-B study and manufacturing, but will be reimbursed by CSL until the senior partner takes over production.

Milestones of "over $300m" will be due relating to regulatory progress and first commercial sale, Uniqure revealed on an analyst call last night, but the real benefits kick in later: a double-digit sales royalty up to the low-twenties percent.

It will be up to CSL to do the heavy lifting for etranacogene dezaparvovec in the market – a setup that makes perfect sense. CSL has a huge presence in blood therapeutics, sourcing blood plasma, and selling intravenous immunoglobulin and, before the patent expired, recombinant factor VIII Kogenate for haemophilia A.

Its Australian stock exchange-listed shares have been on a near-uninterrupted eight-year climb, also thanks to success with the hereditary angioedema drug Haegarda.



That said, CSL is undoubtedly a lower-profile player than the likes of Sanofi, Pfizer or Novo Nordisk, which were seen as possible takeover suitors (*Why Novo Nordisk should buy Uniqure, October 11, 2019*). Neither does it have any experience of trying to sell a gene therapy.

Uniqure had done little to disabuse the sellside of its takeover thesis, and accordingly today some analysts' disappointment was palpable. Mizuho, Wells Fargo and Evercore ISI downgraded the stock, with the latter admitting it had not seen the CSL deal coming.

Etranacogene dezaparvovec aims to become the first gene therapy for haemophilia B, ahead of Pfizer/Roche's fidanacogene elaparvovec. The latter had been originated by Spark, which did succumb to a takeover, by Roche; subsequent documents revealed an unnamed "party B" that had bid $450m up front for a collaboration over Spark's haemophilia A projects, and this might have been CSL.

Gene therapies for haemophilia B				
Company	**Project**	**Approach**	**Status**	**2026e sales ($m)**
Uniqure/CSL	Etranacogene dezaparvovec	AAV5 FIX-Padua gene therapy	Phase III	740
Roche (ex Spark)/Pfizer	Fidanacogene elaparvovec	Factor IX gene therapy	Phase III	35
Freeline	FLT180a	Factor IX gene therapy	Phase II/III	–
Sangamo	SB-FIX	Zinc finger factor IX gene therapy	Phase I	31
Takeda (ex Shire)	TAK-748	Factor IX gene therapy	Phase I/II	–
Logicbio	LB-101	Factor IX gene therapy	Preclinical	29
Applied Stemcell	ASC-519	Factor IX gene therapy	Preclinical	–
Source: EvaluatePharma.				

Perhaps bidders were wary of buying Uniqure because of concerns over the patents backing etranacogene dezaparvovec, which is based on the Padua factor IX variant; the IP here was once described by Spark as "somewhat confused". Uniqure had switched to this Padua variant after first working on wild-type factor IX in a less impressive gene therapy coded AMT-060.

The latest data from etranacogene dezaparvovec's phase II trial were presented at December's Ash conference: factor IX activity in the three patients was 31%, 41% and 50% of normal one year after a single administration of the gene therapy, with no bleeding events reported. The pivotal Hope-B study is to read out this year.

Having licensed out its lead asset Uniqure will be left with an early pipeline whose most advanced gene therapy is AMT-130, in phase I for Huntington's disease. The haemophilia A project AMT-180 has been discontinued, Uniqure revealed, because of "data, regulatory feedback and the evolving competitive landscape".

Perhaps that discontinuation was another reason for this morning's investor disappointment.