Evaluate Vantage

December 22, 2017

Ignyta investors have the last laugh

Jacob Plieth

Ignyta played second fiddle to Loxo for most of the two companies' parallel existences on Nasdaq, but it all changed last month when Bayer struck a deal with Loxo that fell well short of bullish buyout expectations. And today Ignyta completed the surprise rout of its rival by selling itself to Roche for $1.7bn.

It seems that, ultimately, differences between Loxo and Ignyta's tumour-agnostic approaches were nothing more than minutiae. What won the day was a depressed valuation for Ignyta that enabled Roche to see sense in a takeover deal that still offered a 74% premium to the previous day's close.

Valuation must have played a major part in the transaction since Roche is known to be a cautious buyer. The buyout now puts the spotlight squarely on Ignyta's entrectinib, a tyrosine kinase inhibitor found to be efficacious in tumours harbouring Ros1 or NTRK fusions.

Ros1 is, like the related Alk mutation, mainly seen in lung cancer – a setting where Pfizer's Xalkori is the incumbent. Entrectinib is one of a group of Xalkori competitors that are known to cross into the CNS, and thus hold the potential to treat brain metastases (*World Lung – Ignyta's chance to make up lost ground on Loxo, October 18, 2017*).

In NTRK meanwhile, it has been Loxo all the way, with data presented at Asco showing the company's larotrectinib to have activity across 17 cancer types whose only common feature was the presence of a TRK fusion. A rolling US filing for larotrectinib has already been initiated, and Loxo also has a related asset, LOXO-195, which might be used in subjects relapsing on larotrectinib or entrectinib.

Ros1 attraction

Still, it is probably a fair assumption that NTRK – a niche oncology area – is not the driving force behind Roche's Ignyta buyout. The more likely attraction is Ros1, where larotrectinib is not active.

This is because of the way that Xalkori opened up the market in Alk and later Ros1-mutated lung cancer. Roche's CNS-crossing drug Alecensa quickly emerged as a challenger to Xalkori in the Alk setting, but Alecensa seems to have no activity in Ros1, a use for which Xalkori secured additional approval last year.

Thus it is likely that Roche saw Xalkori revenues as ripe for the picking, and wanted to get its hands on an agent with strong Ros1 activity to supplement Alecensa; with Pfizer's lorlatinib looking like the only other Ros1-active asset beyond Xalkori and entrectinib, Roche thus saw sense in buying Ignyta while this company's price was still affordable.

None of this is to say that Loxo is finished; true, a long-awaited buyout has failed to materialise, but with Bayer the group secured $400m up front, and stands to receive nearly as much again in milestones by the end of 2018. Moreover, Bayer has moved quickly to reveal aggressive goals for the Loxo assets (*Bayer's big ideas for star Loxo assets, December 5, 2017*).

And as a sign of interest in this space the activity is also good news for the originators of larotrectinib and entrectinib, Array and Nerviano respectively, and for Mirati Therapeutics, which in sitravatinib has an asset targeting TRK and Ret mutations.

But Loxo has been a victim of its own success. Some of the group's investors will now spend a miserable Christmas bemoaning the fact that bullishness effectively priced their company out of the takeover market.

To contact the writer of this story email Jacob Plieth in London at jacobp@epvantage.com or follow @JacobPlieth on Twitter

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754