Evaluate Vantage

March 18, 2015

Ignyta: boldly going where no one has gone before

Jonathan Gardner

Ignyta, a relatively low-profile US biotech that had so far been notable mainly for its attempt to incorporate Star Trek themes into clinical trial names, warped to a new position in the biotech industry firmament yesterday with a deal to acquire the majority of Teva's small-molecule oncology projects.

The company took advantage of the Israeli group's decision to exit cancer R&D last year to acquire four compounds for a seemingly bargain $12m price. Not only did Ignyta pay for the compounds in stock, it persuaded Teva to invest a further $15m as part of a concurrent $42m financing. Plans for an expansive, mutation-driven lung cancer study to test Ignyta's newly expanded pipeline should be enough to keep investors interested.

Investors welcomed the deal, sending Ignyta's stock up 15% today which, adjusting for the new shares issued, boosts the company's market cap from $155m to $225m.

Five-year mission

Ignyta sees its mission as developing highly targeted compounds with companion diagnostics that can identify patients with specific cancer-driving mutations, an approach it calls precision oncology.

Before the deal, Ignyta had just one clinical asset, entrectinib, which entered the STARTRK-1 phase I/II study last year. The project is an inhibitor of Trk A, Trk B, Trk C, ROS1 and ALK, and the study is recruiting cancer patients confirmed as having one of these specific mutations. It was licensed in 2013 from Nerviano Medical Sciences, an Italian biotech whose main claim to fame is that it is supported (indirectly) by the Vatican.

The acquisition from Teva's portfolio adds a second clinical compound, as well as three late preclinical assets, effectively trebling the size of Ignyta's R&D portfolio. The new clinical asset CEP-32496, now renamed RXDX-105 is a small-molecule inhibitor of BRAF, EGFR and RET. It is in a phase I/II trial that will recruit patients with advanced melanoma and metastatic BRAF-mutated colorectal cancer.

The three pre-clinical compounds are RXDX-106 (CEP-40783), a pseudo-irreversible inhibitor of AXL and cMET, RXDX-107 (CEP-40125), a nanoformulation-modified bendamustine, and RXDX-108 (TEV-44229), an inhibitor of the atypical kinase PKCiota. Bendamustine, sold by Teva under the brand name Treanda, is an established agent approved for the treatment of CLL and lymphoma, and Ignyta thinks the novel formulation could be suitable for solid as well as liquid tumours.

Ignyta will have to assume Teva's obligations to third-parties for the purchased programmes. RXDX-105 and RXDX-106 were both licensed from Ambit, a US biotech that was acquired by Daiichi Sankyo last year. Ignyta will have to pay Daiichi up to $44.5m of development, regulatory and sales milestones for RXDX-105, and up to $47.5m for RXDX-106 as well as tiered royalties. Ignyta described these terms as manageable and consistent with those of its earlier licensing deal for entrectinib.

Warp drive

Alongside the deal Ignyta unveiled plans to initiate a STARTRK-2 trial in non-small cell lung cancer, where patients will be profiled for driver mutations and allocated, as appropriate, to entrectinib, RXDX-105, RXDX-106, RXDX-107 or RXDX-108. This looks like an ambitious study that will test pretty much all of its pipeline in one trial.

To be successful, however, entrectinib will have to navigate around the two approved ALK inhibitors – Pfizer's Xalkori and Novartis's Zykadia – as well as others in development, although its triple mechanism is likely to be a differentiating factor. Pfizer's dual ROS-1/ALK inhibitor PF-06463922 and Tesaro's ALK/TRK inhibitor TSR-011, both of which are also in Phase I/II, are probably the main competitive threats.

For RXDX-105 the competitive environment is more complex. Combinations of BRAF/MEK inhibitors being studied for BRAF V600E-positive NSCLC comprise Novartis's Talfinar and Mekinist, and Array's encorafenib and binimetinib. Four already approved tyrosine kinase inhibitors are being explored in RET fusion positive

NSCLC: Exelixis’s Cometriq, AstraZeneca’s Caprelsa, Ariad’s Iclusig and Eisai’s Lenvima.

Nevertheless, with the Teva deal Ignyta has firmly positioned itself as a serious contender in a fast-evolving field. Given how fast the two ALK inhibitors reached the market, successful signals from the STARTRK-2 study could propel it to a new stage. But as one of the smallest of all the companies here, it will have to work hard to stay competitive.

Trial	Setting	ID
STARTRK-1	125 patients with locally advanced or metastatic solid tumours	NCT02097810

To contact the writer of this story email Robin Davison in London at news@epvantage.com or follow @RobinDavison2 on Twitter