Evaluate Vantage

January 29, 2015

CRISPR steps closer to centre stage as AstraZeneca piles in

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Maxed out on CAR-T and looking for the next field of novel and cutting-edge science to capture the imagination of investors? Look no further than CRISPR, the hot gene-editing technology with a rapidly rising profile, into which AstraZeneca swooped today in a pretty big way.

True, CRISPR is at an even earlier stage than CAR-T and its therapeutic applications are considerably further from the market. But the fields are connected – some CAR-T companies are using gene-editing techniques – and also display similarities; the largely academic-led space has been born of much scientific cross-fertilisation, and IP squabbles loom large. As long as the stock markets remain so receptive to risk, it will surely not be long before public investors can get involved.

Currently there are only three companies, all private, that have declared a dedication to the use of CRISPR to develop drugs: Editas Medicine, Intellia Therapeutics and Crispr Therapeutics.

CRISPR, a third-generation gene-editing technology, follows in the wake of zinc finger and TALEN platforms. The idea is the same, although rather than using large, unwieldy proteins to guide a DNA-cutting enzyme to its target, like the earlier incarnations, CRISPR uses tiny strands of RNA. The result is a much more precise tool that allows multiple genetic deletions or edits to be made, with huge implications for the cost and time of experiments.

So it is not surprising that CRISPR has attracted a fair amount of commercial interest in a very short space of time. Researchers first demonstrated that RNA could be used in this way at the end of 2012, and the following year the finding was translated from the test tube to living cells.

Snowballing

As with the CAR-T space, several scientists at various academic centres have dominated the development work, and few have wasted time setting up commercially focused enterprises to develop CRISPR's potential. And much of the IP is still controlled by their institutions.

Editas, for example, was founded in late 2013 by five scientists who pioneered much of the early work. Although the company has a stated aim to translate its technology into therapeutics, a pipeline has yet to emerge, and it seems likely that much of the $43m series A funding it secured has been invested in establishing its IP position.

In December, it unveiled licensing deals with various academic institutions over their respective technologies, most of which were associated with the company's founders, including the Broad Institute and Harvard University.

Last November Intellia Therapeutics was launched with a $15m series A financing; it was created by Caribou Biosciences, Atlas Ventures and Novartis, to exclusively exploit the former's CRISPR technology platform for human gene and cell therapies.

Novartis has already forged a formal collaboration with Intellia giving the Swiss pharma giant access to its technology, along with tasking Intellia to look at using CRISPR to engineer CAR-Ts and haematopoietic stem cells.

In a sign of just how tightly interwound this field is, one of the founders of Caribou, Jennifer Doudna, of the University of California, is also a scientific founder of Editas. She was a collaborator with Emmanuelle Charpentier of the Helmholtz Centre for Infection Research in Germany, who co-founded Crispr Therapeutics, the third main corporate player. The Swiss and UK-based company raised $25m last year.

So for those with their eyes firmly on the clinic, it seems likely that lengthy IP negotiations await. In this way the field does look much like the CAR-T space, which is perhaps ironic given that these cellular therapies will naturally lend themselves to some of the first therapeutic applications of CRISPR.

The Novartis deal with Intellia suggests as such – Novartis being the biggest big pharma CAR-T player – while in November last year Johnson & Johnson forged a deal with Transpogen, which is using CRISPR to create off-the-shelf T cells that include the all-important chimeric antigen receptor.

Into the mainstream

For others interested in the potential, at this stage CRISPR seems likely to be viewed much more as a research tool. Most of the big services companies like Sigma-Aldrich and Agilent now offer CRISPR tools, and aspects of AstraZeneca's new collaborations, which include one with Thermo Fisher Scientific, appear geared to this direction.

However the UK pharma company also professed a desire to harness "the power of CRISPR" across its entire discovery platform, suggesting that it holds out hope for more immediate breakthroughs. It also unveiled deals with the Wellcome Trust Sanger Institute in Cambridge, for access to its guide-RNA library, and the Innovative Genomics Initiative in California and the Broad Institute in Massachusetts, where much of the pioneering CRISPR work has been done.

For all of AstraZeneca's clear commitment, it seems more likely that the first therapeutic applications of this technology will emerge from the start-ups that have sprung from these institutions. But everyone working in this space has some way to travel, and CRISPR itself is likely to evolve in the meantime. The emergence of rival gene-editing technologies also cannot be ruled out.

Investors might not have another CAR-T bandwagon to jump on just yet. But the outline is forming, and it would probably only take a couple of projects to move towards the clinic to get the wheels rolling.

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