Evaluate Vantage

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Gilead deal shows desire to put oncology at centre of post-Hep C strategy

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Gilead's acquisition yesterday of a small Danish oncology start-up, EpiTherapeutics, was clearly not the Pharmacyclics-like M&A event that analysts have been looking for, but it is probably more important than its modest $65m price tag suggests.

This is not so much for what EpiTherapeutics provides – a library of early-stage, small molecule inhibitors of epigenetic regulation – but for what it signals, namely a renewed commitment to make oncology the centrepiece of the company's long-term growth strategy.

As successful as Gilead undoubtedly has been with Solvaldi and Harvoni, these key products are set to mature in the late 2020s, and the group needs a solid strategy to maintain sales growth when competition, decreasing patient numbers and/or loss of patent exclusivity are expected to cause its hepatitis C franchise to falter.

Go with the growth

Unsurprisingly, Gilead has plumped for expansion into the industry's biggest growth sector, oncology, but analysts had become concerned the plan was looking a little threadbare, especially in the context of a treatment landscape likely to be dominated by checkpoint inhibitors and CAR-T therapies.

Gilead's cancer franchise centres on Zydelig, which was last year approved for certain settings in chronic lymphocytic leukaemia, follicular B-cell non-Hodgkin's lymphoma and small lymphocytic lymphoma, while the rest of the cancer pipeline (see below) consists of seven compounds, mostly small molecules, with a bias towards haematological indications.

And while Zydelig is making reasonable progress on the market, it is facing formidable competition in the form of J&J/AbbVie's Imbruvica, a drug whose expected dominance of the lymphoma/leukaemia field could be further strengthened by combination with AbbVie/Roche's GDC-0199/ABT-199. *EvaluatePharma* consensus forecasts suggest Zydelig sales will reach $835m by 2020, very small beer compared with the $5.5bn predicted for Imbruvica in the same year.

Bolt on not big

Gilead's cancer pipeline has to date been built up almost entirely by acquisition – Zydelig was obtained with the $375m purchase of Calistoga Pharmaceutical in 2011, while momelotinib was obtained via the $510m purchase of YM BioSciences in 2012 – so analysts have been looking for an eye-popping M&A deal that cements its position in this field. It looks like they will continue to wait, but in the meantime the EpiTherapeutics acquisition should not be overlooked.

The deal gives Gilead a strong position in the emerging field of epigenetics - the study of how environmental factors alter the activation of certain genes – together with a number of small molecule inhibitors of epigenetic regulation of gene transcription, in particular the relatively unexplored area of histone demethylases. The field of epigenetics has been of interest to big pharma for a long time, but has to date proved disappointing, generating to date only two classes of approved drugs: histone deacetylase (HDAC) inhibitors and DNA methyltransferase inhibitors.

EpiTherapeutics, which was a spin-out from the University of Copenhagen, is one of a handful of companies developing histone methyltransferases or histone demethylases, and this puts it in a group with Epizyme and Constellation Pharmaceuticals, although both of these are further ahead.

Combination therapies

Gilead did hint at its rationale for the acquisition in the comment that EpiTherapeutics portfolio has the potential for it to develop novel combination approaches. This could help a number of its compounds in the longer term. Zydelig is likely to face competition not only from Imbruvica but from AbbVie/Infinity's duvelisib, a PI3K delta/gamma inhibitor, which is in two phase III studies for follicular lymphoma and relapsed/refractory CLL/SLL.

However, despite what looks like a very low-risk, strategic play what Gilead could still do with is an M&A deal that silences its critics and gives it a much larger stake in cancer drugs, especially immuno-oncology. Such a deal would undoubtedly be on the scale of Pharmacyclics, but Gilead has shown it can do such deals successfully. But, given Gilead's oncology deal track record so far analysts may have to wait a little longer for this deal to materialise.

Gilead cancer pipeline			
Compound	**Mechanism**	**Indication**	**Stage**
Zydelig	PI3K delta inhibitor	Frontline and relapsed refractory CLL	Phase III
		Relapsed /refractory iNHL	Phase II
Momelotinib	JAK inhibitor	Myelofibrosis	Phase III
		Pancreatic cancer	Phase II
Entospletinib	Syk inhibitor	Haem malignancies	Phase II
		AML	Phase I/II
		ALL	Phase I
GS-5745	MMP9 mAb inhibitor	Gastric cancer	Phase II
GS-4059 /Ono-4059	BTK inhibitor	B-cell malignancies	Phase II
GS-5745	MMP9 mAb inhibitor	Solid tumours	Phase I
GS-9901	PI3K delta inhibitor	Haem malignancies	Phase I
GS-5829	BET inhibitor	Solid tumours/DLBCL	Phase I

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