Gilead making smart early moves in a new direction

Following a less than successful strategic move into cardiovascular therapies, Gilead Sciences is now determinedly trying its hand in oncology and inflammation (Gilead has little to show for its expensive CV push, December 15, 2009). The acquisition of cancer drug developer Calistoga Pharmaceuticals for up to $600m follows hot on the heels of the Arresto Biosciences and CGI Pharmaceuticals buys last year, clearly highlighting a new direction for the HIV specialist.

None of these companies have products anywhere near the market and will require significant investment in the coming years. Gilead might have little experience in these new fields but funds are certainly not a problem - its HIV franchise generates billions of dollars of cash each quarter and new sources of revenue need to be found for the future. Still, Gilead shares dropped 2% on the news yesterday, despite broad agreement that Calistoga brings some very promising compounds. This new direction will take time and money, and although Gilead has plenty of the latter investors will want to see it better spent this time around (Gilead hurt by faltering confidence, July 19, 2010).

Promising oncology asset

Using its cash-in-hand, Gilead will pay $375m for Calistoga, with potentially a further $225m in payments for reaching certain milestones, as yet undisclosed.

Gilead has gained a potentially valuable asset in CAL-101, a haematological cancer drug that some believe could be filed early, on data from a phase II trial started earlier this year.

The drug inhibits the delta isoform of phosphatidylinositol 3-kinase (PI3K), a well-studied target in cancer because it is central to the proliferation, growth and mobilisation of tumour cells. The PI3K pathway also plays a role in inflammation, and as such Calistoga has based its pipeline on this pathway, including phase I anti-inflammatory and autoimmune disease candidate CAL-263.

In an interview last year with EP Vantage, Calistoga’s chief executive Carol Gallagher reckoned no other PI3K inhibitors demonstrate the same levels of safety and efficacy as CAL-101 (EP Vantage Interview - Calistoga eying registration trials with new funds, July 22, 2010).

Promising activity

CAL-101 has shown good activity so far in the clinic – analysts point to a 48% response rate in mantle cell lymphoma, and 63% in refractory indolent non-Hodgkin's lymphoma (iNHL). And as it specifically inhibits the delta form of PI3K, CAL-101 could have an important advantage in terms of safety over similar drugs such as Exelixis’ XL147 and Roche’s RG7321, targeted at multiple isoforms of PI3K.

Analysts at Leerink Swann, who describe CAL-101 as “one of the more promising emerging oncology assets”, reckon the candidate could be filed in 2013 if strong data are reported from the phase II study started this year, as a single agent in iNHL patients refractory to Rituxan and alkylating agent-based chemotherapies. Preliminary results may be available in October next year.

Another mid-stage trial of CAL-101 in combination with Rituxan in treatment-naïve, elderly chronic lymphocytic leukaemia (CLL) patients is ongoing, although this is not expected to report preliminary results for another couple of years.

Gilead has indicated it plans to start registration trials with CAL-101 this year in both indications.

Long term investment

Calistoga has long been regarded as a company to watch in oncology, and this move has been widely applauded by analysts. It follows Gilead’s acquisition of CGI Pharmaceuticals last year that brought some early stage spleen tyrosine kinase (Syk) inhibitors and Arresto, which develops medicines that target enzymes involved in fibrotic diseases and cancer (Gilead gains one and loses one in IPF, December 24, 2010).

Compared to when it tried to break into the CV space Gilead is clearly taking a different tack this time. Rather
than buying companies with products already on the market – CV Therapeutics was already selling Ranexa and Lexiscan and and Myogen had launched Letairis – it is targeting much earlier stage projects this time round.

It spent $3.9bn buying those two firms. This push has cost it $720m so far, although Calistoga could cost another $225m down the road.

Of course expanding into oncology and immunology will not come cheap, and could well ultimately cost more when spending on development over the years is taken into account. These initial moves look smart, but only time will tell whether a new early stage strategy will pay greater dividends.