Evaluate Vantage

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Upcoming events: pacritinib in myelofibrosis and an adcom for Kythera

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Welcome to your weekly digest of approaching regulatory and clinical readouts. By the end of the first quarter CTI Biopharma is expected to report topline phase III results of pacritinib in myelofibrosis. Jakafi might be the current market leader but it suffers from safety concerns, increasing the opportunity for new improved agents.

Meanwhile, Kythera's fat buster ATX-101 will come under scrutiny from an FDA panel on March 9. Kythera has two positive phase III trials behind it, and while analysts expect approval the panel is likely to scrutinise safety. Although it lost Bayer as a partner last year, Kythera could make the the aesthetic giant Allergan take notice with a positive advisory committee vote.

Pacritinib: CTI Biopharma/Baxter

Topline results from pacritinib's pivotal phase III trial called Persist-1 are expected before the end of March. The trial is in 322 patients with myelofibrosis, polycythaemia vera or thrombocythaemia, testing pacritinib, a JAK-2/FLT3 inhibitor, versus best available therapy excluding marketed JAK inhibitors.

The primary endpoint is the percentage of patients achieving a reduction in spleen volume of 35% or more, assessed using by MRI or CT, following 24 weeks of treatment. A second trial, Persist-2, could be more interesting for investors; it will test pacritinib against therapies that this time include JAK inhibitors. Enrolment is expected to be completed by mid-2015.

Pacritinib was originally licensed by S*Bio to Onyx Pharmaceuticals for $25m up front in early 2009. Onyx canned the deal two years later after seeing less than stellar phase II data, only for the project to be picked up by CTI Biopharma, then called Cell Therapeutics, in 2012. CTI paid $30m up front, half in cash and half in convertible stock.

This did not stop CTI attracting a partner; at the end of 2013 Baxter paid $60m, including an equity investment in CTI of $30m, for joint US and full ex-US rights. Since then, CTI has received a $20m milestone payment from Baxter for completing enrolment in Persist-1, and a further $20m is due if it can do the same in Persist-2.

The myelofibrosis market is dominated by the first drug introduced specifically for this disorder, the JAK-1/2 inhibitor Jakafi from Incyte and Novartis. Its 2020 sales in this indication are forecast to reach $1.2bn, according to *EvaluatePharma* consensus.

Jakafi was approved on the basis of significant improvements in spleen size and total symptom score, even though its use exacerbates anaemia (*Therapeutic focus – New agents nip at Jakafi's heels in myelofibrosis, October 1, 2013*). This means there is a clear opportunity for an improved agent, particularly in patients who cannot tolerate Jakafi.

ATX-101: Kythera Biopharmaceuticals

Elsewhere, Kythera Biopharmaceuticals' ATX-101, a treatment for submental fat – better known as a double chin – will go before an FDA adcom.

Analysts are bullish that the project will get a yes vote from the FDA's dermatologic and ophthalmic drugs advisory committee on March 9, and judging by Kythera's share price – up 25% so far this year – investors are optimistic too.

Whether success will materialise depends on how the panel views Kythera's choice of endpoints in its two identical pivotal studies, Refine-1 and Refine-2. The primary outcome was ratings by doctors and patients of improvement in double chin compared with placebo, with the secondary endpoint being far less subjective: reduction in fat volume measured by MRI (*Kythera's chin up following double phase III success, September 17, 2013*).

Both trials met both endpoints, but the FDA's advisors might be easier to convince had the emphasis been on the MRI evidence. Safety could be an obstacle too; the rate of neuropraxia – loss of motor and sensory nerve

function – was 0.6% across all studies. JP Morgan analysts say Kythera sees this rate as “low” and thinks training efforts will lower it further over time.

EvaluatePharma computes consensus 2020 sales of $480m, giving the asset an NPV of $873m – 89% of Kythera's market cap. If ATX-101 is approved on its May 13 PDUFA date Kythera plans to launch it with a 73-strong sales force, with physician training a key component of the launch.

With many of Kythera's executive team having worked at Allergan, investors will be hoping that success prompts interest from the aesthetic giant, now owned by Actavis.

Study	**Trial ID**
Persist-1	NCT01773187
Persist-2	NCT02055781

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