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China comes of age

Jacob Plieth

Chi-Med is not alone in seeing Chinese approval as the prelude to a regulatory green light in the west.

This week's approval of Chi-Med's fruquintinib in China looks like a blueprint for others, and shows just how far the local industry has progressed in establishing the country as a serious manufacturing base with a serious medicines regulator.

It was, after all, just 11 years ago that the former head of China's state FDA was executed for taking bribes to approve untested medicines. But with at least two other biotechs lining up to get drugs approved in China before the US, and cash inflows prompting a China-focused biopharma index to be set up, a line might at last have been drawn under such problems.

One of the first companies to take seriously the issue that production tended to be substandard was Innovent Biologics, which invested specifically in China manufacturing that met western standards. Its reward? $100m, $260m and $150m series C, D and E financings, plus a key alliance with Lilly worth $56m up front.

Innovent's anti-PD-1 MAb sintilimab was filed for approval in China in April, four months before another home-grown asset, Beigene's anti-PD-1 project tislelizumab, was submitted. While the latter is in two pivotal trials that include US hospitals, clinical development of sintilimab in the west has yet to begin.

Chi-Med first

In the event Innovent and Beigene were beaten by Chi-Med's VEGF-R inhibitor fruquintinib, which on Wednesday secured approval for colorectal cancer under the brand name Elunate, becoming the first China-discovered and developed oncology drug to go through formal randomised trials and reach the local market.

Clearly Chi-Med's next regulatory goal is the US and Europe, but for now fruquintinib's most advanced western study is a phase I trial that should be completed the end of this year. After that, an aggressive development programme for US and EU approval will begin, Chi-Med's chief executive, Christian Hogg, told *Vantage*.

While he made it clear that there was no way a Chinese pivotal study could expedite US development, he said results already generated boosted the safety dataset and increased his confidence in fruquintinib's target specificity and path forward in the west. "A lot of the questions have been answered," he stated.

Chi-Med will manufacture Elunate, but the drug will be sold in China by Lilly, which holds a local licence.

It is noteworthy that the US group also has the deal with Innovent, serving as the Chinese group's partner for

the west for several assets including sintilimab, while Innovent's local rights to Lilly's c-Met antibody emibetuzumab represent Lilly's gateway into China.

Lilly also has an option over global fruquintinib rights, exercisable within two months of the expected October readout of a phase III lung cancer trial. However, since Lilly already sells the rival VEGF-R inhibitor Cyramza, “it is very unlikely that [it] will exercise”, said Mr Hogg (*Event – Lilly faces tricky opt-in decision on fruquintinib, March 30, 2017*).

Chinese plans

Presumably if fruquintinib is left on its own outside China Chi-Med will have to seek a new partner. The group also has two other key irons in the fire: savolitinib, licensed globally to Astrazeneca, and the unpartnered sulfatinib.

While the former is being developed in the west and China in parallel, sulfatinib is following fruquintinib’s blueprint: development is more advanced in China, with two phase III trials ongoing, than in the US, where the asset is in late phase I.

There is reason for optimism for this approach, notwithstanding issues around drug affordability and reimbursement that have yet to be worked out properly. And the Chinese regulator has been busy: before greenlighting Elunate it approved Bristol-Myers Squibb’s Opdivo as the country’s first PD-1 inhibitor, and this week gave the thumbs up to Merck & Co/Eisai’s Lenvima.

The money has flowed in, too, resulting in the Hong Kong stock exchange going out of its way to attract biotechs, modifying its listing rules and assembling a biotech advisory panel in April.

And last month the Loncar China Biopharma exchange-traded fund was launched on Nasdaq, offering US investors direct exposure to Chinese stocks including Wuxi Biologics, Beigene and Zai Lab. While Chi-Med and Beigene both have local listings, they are also separately traded in the west, on the London stock exchange and Nasdaq respectively.

True, manufacturing can still be hit and miss – witness the problems Teva has had with its Chinese supplier of valsartan – but several companies seem at last to be on the right track.