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China's Canbridge nabs Puma's Nerlynx for HER2+ breast cancer in $70M deal

By Shannon Ellis, Staff Writer

SHANGHAI – Beijing's Canbridge Life Sciences Inc. has acquired the greater China rights to Puma Biotechnology Inc.'s Nerlynx (neratinib) as an adjuvant for early stage HER2-positive breast cancer and other HER2 tumors, such as gastric cancer, which is highly prevalent in China.

The deal will provide Puma with an up-front payment of $30 million, with the possibility of another $40 million upon regulatory milestones. Royalties and sales milestones could also provide Puma with further payments.

Nerlynx, an irreversible tyrosine kinase inhibitor, was approved by the U.S. FDA in July. But the Los Angeles-based company encountered pushback from Europe's regulators, with the Committee for Medicinal Products for Human Use (CHMP) indicating a negative trend vote last month. (See *BioWorld*, July 19, 2017, and Jan. 25, 2018.)

With poor prospects in Europe, Canbridge remains steadfast about Nerlynx's chances in greater China. "We assessed the opportunity and even with the recent news from Europe, we will not waver in terms of our position to get this product to patients in China," James Xue, Canbridge chairman, CEO and president, told *BioWorld*. "I want to emphasize this is a brand new drug that received U.S. FDA approval in an area that has very little treatment options and has a strong case for us to present to the authorities in our geographies, including mainland China, Taiwan, Hong Kong and Macau."

Nerlynx is approved in the U.S. as an adjuvant for patients using Herceptin (trastuzumab, Roche Holding AG)-based therapy with HER2-positive breast cancer. About 20 percent to 25 percent of breast cancer patients overexpress the HER2 protein.

After a course of Herceptin, patients often have no additional treatment options, explained Xue. Depending on the individual, within about five years a significant number of patients – up to 25 percent – will find the cancer recurs in a very vicious form. Many patients lacking treatment options will die within six months; Xue called it "a very dire situation." In China, that is especially so. "In terms of Chinese patients, the Chinese breast cancers are more aggressive compared to the western form and occur in a younger age group relative to the western patient population," said Xue.

Assessing the global phase III MRCT data from Puma, Xue said a significant number of patients taking Nerlynx had reduced rates of recurring cancer vs. the comparator (according to Puma's release it can be 34 percent). "This is a major accomplishment and clinical benefit for patients who do not have recurring cancer; they will live over five years," Xue said. "And for those with recurring cancer, it allows those patients to have a chance at extended disease-free survival."

Accelerated approval in China possible

The large amount of data that Puma collected in its global pivotal study may help Canbridge seek accelerated approval in China. Post-ICH (International Council for Harmonisation) admittance, China's regulators have said they will accept global data. Since a portion of the data collected by Puma also included Chinese patients and those of Asian ethnicity, there is a chance that Canbridge may be able to seek approval without a clinical study in China, or only a limited one.

"We believe that we will be able to leverage the existing data to a maximum extent for a shortened market approval pathway," said Xue. "We will leverage the data that Puma has already built on a global scale, including Asian patients with their pivotal study. Over 2,000 patients enrolled in the pivotal study over five years – it is one of the most sophisticated studies ever done in breast cancer."

But in Europe, regulators have raised concerns over the clinical relevance and risk-worthiness of Nerlynx in extended adjuvant use for women with early stage, HER2-positive breast cancer and asked for Puma to take "additional steps."

Puma said the CHMP found a benefit-risk assessment for Nerlynx to be negative since it was based solely on evidence from a single pivotal trial and because "two- and five-year invasive disease-free survival benefits observed to date may lack sufficient clinical relevance."

Another factor Canbridge will need to work through when discussing Nerlynx with Asian regulators are the side effects of Nerlynx, including grade III diarrhea. "Puma did a good job to educate us about how they developed effective patient management protocol for the side effects," Xue said. "We looked at the data for the prevalence and seriousness of the diarrhea ... the protocol developed by Puma should be very straightforward for us to adopt in China."

Meanwhile, in the U.S., Puma is seeking to widen the scope of use for Nerlynx to more HER2-expressed cancers in a basket trial for patients with breast, cervical, biliary, salivary and non-small-cell lung cancers.

Canbridge will take the lead on gastric cancer, which is highly prevalent in China. The company will also seek out approval for other forms of HER2-positive cancers as well, including late-stage metastatic breast cancer in China.

Getting market ready

With many of China's regulatory hurdles now lowered, Canbridge, like many Chinese biotech startups, is getting market ready for the first time. The firm's plan is to see Nerlynx on the market by mid-2019. In advance of that, Canbridge's CAN-002 for mucositis caused by radiation or high-dose chemotherapy should receive CFDA approval.

"The timing of this deal is excellent in terms of building a full-fledged commercial presence which is already underway," said Xue. "This is transformative because it accelerates our vision to build a virtually integrated company from development to full commercialization. My team and I are very excited about Puma's decision to choose us as a partner. We want to be

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> Chairman, President/CEO, Canbridge

known as the partner of choice in China and greater Asia area for such opportunities."

The remainder of Canbridge's pipeline is more early stage. CAN- 008 for glioblastoma multiforme is already in phase I trials in Taiwan. The biotech holds the greater China rights for CAN-008, which has been designated a MAH (marketing authorization holder) pilot project in China where it is seeking an IND. In addition, Canbridge's CAN-017 is also seeking an IND in China for squamous cell esophageal cancer. Canbridge holds global rights for CAN-017, excluding North America. ♦,