# **Press Cutting**

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## **Strategy**

# Met-ing the neighbors

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AstraZeneca pic's grassroots approach to business development in Asia has allowed it to bring in a program from Hutchison MediPharma Ltd. that was under the radar of analysts covering the Chinese company. The deal to develop an inhibitor of c-Met receptor tyrosine kinase also provides the first validation of the 10 years and almost \$100 million the Chinese blotech has spent building its In-house

discovery operations.

Hutchison MediPharma was established in 2002 to screen Chinese traditional medicines in search of pharmaceuticals. The company is a subsidiary of U.K.-listed Hutchison China MediTech Ltd. (Chi-Med), which listelf is a unit of Hong Konglisted multinational conglomerate Hutchison Whampoa Ltd.

"People probably don't realize that Hutchison MediPharma has been in place

In Shanghal now for 10 years because of our structure as a subsidiary of a subsidiary, both of which are listed companies," CEO Christopher Hogg told BioCentury. "Hutchison Whampoa is better known as one of the largest telecommunications and port services companies in the world, so the fact that our work as their foray into pharmaceuticals is non-core and not even adjacent is one reason we've been relatively quiet."

Despite the low profile, Hogg said Hutchison MediPharma is one of the few biotechs with an established presence in China.

He attributed the paucity of Chinese innovator biotechs to "there being so much other low-hanging fruit here, like internetand consumer-related areas — or even CROs — where the investment horizons are shorter, so venture investors have been less interested in funding pure research and innovation."

Hutchison MediPharma didn't need to chase VC money because it had a deep-pocketed parent. This gave the company "a five to seven year head start" on biotechs doing in-house R&D in China, Hogg said.

Its first-mover status allowed it to attract some of the "most experienced Chinese pharma executives, many of whom had gone to the U.S. for education and ended up working at big biotechs or pharmas in the U.S. or Europe," he said.

"Based on the experience of the team we decided we wanted to go beyond botanicals," Hogg said. "Starting in 2004-05 we began focusing on small molecule drug discovery" with an emphasis on oncology and inflammation.

'Hutchison MediPharma now employs 200 full-time scientists, 120-130 of whom are focused on In-house discovery.

"We see ourselves as a fully integrated operation able to discover compounds, optimize and take them through preclinical development. Then we have a clinical and regulatory group capable of managing China-based clinical trials," said Hogg.

Last month's deal with AstraZeneca to co-develop and commercialize volitinib (HMPL-504) is the first partnership for one of Hutchison MediPharma's in-house small molecules.

The companies will share development costs in China, while

AstraZeneca will be responsible for development in the rest of the world. Hutchison MediPharma will receive \$20 million up front and is eligible for \$120 million in development and initial sales milestones, as well as additional sales milestones and up to double-digit royalties.

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"Volitinib has better selectivity and is more potent relative to what else is out there in the clinic, so we expect that it will differentiate itself in the clinic," said Hogg.

Phase I testing will begin "Imminently," he said.

AstraZeneca will wait to see undisclosed data from the clinical program in China before deciding whether to pursue volitinib elsewhere, said Detlev Biniszklewicz, VP of strategy and external alliances in AstraZeneca's oncology IMED (innovative medicines unit).

The most advanced c-Met Inhibitor is Pfizer Inc.'s Xalkori crizotinib, a dual Inhibitor of c-Met receptor tyrosine kinase

and anaplastic lymphoma kinase (ALK) and their oncogenic variants. The drug is approved for advanced or metastatic non-small cell lung cancer (NSCLC) in patients whose tumors are ALK-positive.

Behind Xalkori are tivantinib (ARQ 197) from ArQuie Inc. and cabozantinib (XL184) from Exelixis Inc. The molecules are in Phase III testing for NSCLC and thyroid cancer, respectively. Tivantinib is partnered with Dalichi Sankyo Co. Ltd. and Kyowa Hakko Kirin Co. Ltd.

## Going local

In 2006, AstraZeneca unveiled plans to put \$100 million towards establishing the Innovation Center China (ICC) in Shanghal, which has become the company's regional R&D base.

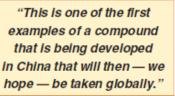
Indeed, Biniszkiewicz suggested the volitinib deal was made possible only because of pharma's presence in China.

"Somebody from ICC walked down the street to Hutchison and talked to them about what it was they were working on," which is the only reason AstraZeneca was made aware of volitinib, he said. In fact, "I spoke with several analysts who cover Hutchison earlier this month who told me they hadn't even known about this program since it wasn't in the clinic yet."

AstraZeneca already was interested in bringing in a c-Met program. "This is one of the first examples of a compound that is being developed in China that will then — we hope — be taken globally," said Biniszkiewicz.

"China is one of the pockets of innovation that a lot of companies are talking about but almost nobody has really utilized very much," he added. "We have built a very good network of alliances within Asia, and China specifically, where we have agreements with hospitals and research centers that provide us with insight into the emerging scientific innovation."

As part of this effort, AstraZeneca has research collabora-



Detlev Biniszkiewicz, AstraZeneca

tions with academic institutions in Beijing, Shanghai and Guangdong focused on gastric, liver and lung cancers, respectively.

## Branching out

Late last year, Hutchison MediPharma brought in its first two outside investors. In November, Mitsul & Co. Ltd. received a 12.2% stake in exchange for a \$12.5 million investment and SB China Venture Capital Ltd. took an undisclosed stake one month later.

The two investors were brought in "to establish a 'stake-inthe-ground' on the valuation of Hutchison MediPharma," according to Hogg. "We were able for the first time to put a concrete valuation on the company, which was important for confidence and validation for Chi-Med investors, including Hutchison Wampoa."

The investment deals pegged the pre-money valuation at \$82 million. he noted.

Rather than bringing in additional strategic or venture investors, "we'd prefer to fund ourselves through partnerships like the recent deal with AstraZeneca rather than dilutive equity fundraisings," Hogg added.

Hogg hopes Hutchison MediPharma can churn out one to two clinical candidates each year.

The company's lead in-house program, HMPL-004, emerged from work with an undisclosed Chinese herb. It is a botanical extract that inhibits a variety of inflammatory cytokines in the NF-kB pathway, exerting its primary effects on tumor necrosis factor (TNF) alpha, IL-1 and IL-6.

In a placebo-controlled Phase IIb trial in 223 patients with mild to moderate ulcerative colitis (UC), HMPL-004 met the primary endpoint of clinical response. The endpoint was assessed based on quantitative symptom reduction using standard Mayo scoring as well as a decrease in rectal bleeding (see BioCentury, Nov. 23, 2009).

In oncology, Hutchison MediPharma's small molecule discovery is directed against targets involved in angiogenesis, the cell cycle and signal transduction. Hogg said the company is focusing on proteins that academic publications suggest are associated with cancers particularly prevalent in China and Asia, including gastric and NSCLC.

Its pipeline now includes five molecules that Hogg described as in or on the verge of Phase I testing.