Pfizer Unveils Upjohn Global HQ In China Amid Unprecedented Pricing Pressures

Executive Summary
In an effort to get closer to customers, Pfizer opens Upjohn global headquarters in Shanghai amid a fast-changing environment, the US-China trade standoff and potentially increased price erosion.

Getting closer to customers and responding to local needs fast is what executives had in mind as they decided last year to locate the global headquarters of Pfizer Inc.'s established products unit, Upjohn, in Shanghai, the hub of the pharma industry in China.

With a fast-aging population and rising incidence of chronic diseases, success in the country is critical to a suite of 20 mature Pfizer products, ranging from the antihypertensive Norvasc (amlodipine) and cholesterol drug Lipitor (atorvastatin) to pain treatments Celebrex (celecoxib) and Lyrica (pregabalin).

The move is a bold one. Out of a total of 12,000 Upjohn employees, 5,000 will be based in China, including at the new Shanghai base, a formulation and manufacturing plant in the northeast city of Dalian and at sales and marketing networks across the country.

But there are also some ominous signs around the timing. While Pfizer made the decision to choose China's commercial megacity as its global anchor last July, nearly one year later the US drug maker is facing a much different environment in China, both commercially and policy-wise.

First, the country late last year initiated the massive “4+7” centralized bidding mechanism in major cities for dozens of widely prescribed off-patent drugs, including multiple statins and other cardiovasculars against which Pfizer Upjohn products are currently competing.

Then the trade dispute between China and the US, which started around a year ago, has now escalated significantly, with trade negotiations breaking down and no immediate end in sight.

Does China still offer attractiveness for such a large-scale corporate move? Executives think so. “China is critical for us,” noted Michael Goettler, group president of Pfizer Upjohn, during an opening ceremony in the brand new Shanghai headquarters on 30 May.

Calling Shanghai a strategic location, the CEO said the China decision would allow the company to respond to local needs fast and to attract talent in an increasingly competitive market.

Embracing The Storm
To combat the impact of the 4+7 bidding mechanism, Pfizer Upjohn has cut prices for some of its best-selling drugs in China and is adding more resources to explore the so-called broad market in smaller cities.

The price of Lipitor has been reduced by 30% but the drug still lost out in the bidding process to domestic maker Jialin Pharma, a subsidiary of Luye Pharma, which slashed its atorvastatin price by 83%.

Pfizer hopes the price cut will still be able to attract more self-pay patients, offsetting the negative impact. “We didn't win the bid in the 11 cities process,” noted Goettler, adding “the volume is expected to decrease.”
Lipitor is the top-selling product in China, growing by 16% in 2018, according to IQVIA data collected from hospitals with over 100 beds. Combined with a similarly strong showing for Norvasc, it has propelled Pfizer to the ranks of top multinational pharma firms in China. (Also see “Calm Before The Storm: Pharma Opens 2019 With A Bang In China” - Scrip, 9 May, 2019.)

In other provinces such as Hubei, where the 4+7 process has not yet started, Pfizer is also reportedly lowering prices of 15 products, ranging from 3.4% to 10.2%. Going forward, the company said it can’t predict further cuts.

**Deepening ‘In China, For China’ Approach**

The ongoing US-China trade dispute, which has had only limited impact so far on the health products sector, has prompted more US companies to adopt an “In China, For China” strategy, noted a recent business survey.

As many as 35% of American companies in the country are adopting localized manufacturing and sourcing to mainly serve the China market, noted the American Chamber of Commerce (AmCham) in China in a survey released 22 May. “Such strategy constitutes a rational choice for many companies to insulate themselves from the effects of tariffs while maintaining their ability to pursue domestic market opportunities,” it noted.

Despite pharma being less impacted by the raising of tariffs, the lingering trade war could eventually disrupt the business, noted Goettler.

Roughly one quarter of surveyed businesses said the increases so far in US and Chinese tariffs were having no impact, but 43% of AmCham members supported a return to the status quo, showing that members want a trade deal and a return to the pre-tariff predictability and stability in the US-China trade relationship.

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**Going Beyond The Pill**

Despite the focus on price-cutting and volumes, Pfizer Upjohn executives emphasized at the opening increasing efforts to go beyond the pill. “Price is not the first concern,” stressed Goettler, who added that improving patient awareness and deepening the In China, For China strategy form part of the larger picture.

Despite years of uncovering patient needs, demand in China for cardiovascular treatments remains large. One signature program run by the company is “Bending the Curve”, a multi-year partnership started seven years ago between Pfizer China and China’s health ministry. This is designed to raise awareness, patient education and early screening for cardiovascular conditions including hypertension and strokes.

In a bid to sharply cut rising mortality rates from cardiovascular diseases, the program includes large-scale screening of populations with high-risk factors. While incidence and mortality have turned downward in the US, these keep rising in China and the multi-year initiative aims to turn the tide.

The goal is to reach out to millions with conditions that have not been diagnosed and treated, and in the meantime to expand the reach of therapies from large cities to lower-tier cities, the so-called broad market that has yet to be fully tapped. (Also see “Merck KGaA, Pfizer Dance To China Digital Health Beat” - Scrip, 29 Jan, 2019.)

There is unmet need “not only in rural areas but also in big cities...we believe we can be part of the growth going forward,” Goettler told reporters during a press round table at the opening. To that end, the company is adding 600 staff in 2019 to further explore China’s broad market segment.

With annual cardiovascular patient numbers exceeding 270 million in China - meaning one in five adults suffer from such disorders and roughly
three million associated deaths - the need for early diagnosis and preventative care seems huge.

Despite the company having previously partnered with Sinopharm to reach out to lower-tier cities and counties, “We are big in big cities but small in small cities,” conceded Tianxiang Miao, Pfizer China’s general manager. To change that, he said the company will combine digital tools with additional on the ground sales people.

Predicting “turbulence in the short term,” Miao said closely aligning with the central government’s Health China 2030 strategic plan would be key to success in China’s fast-changing environment. Pfizer’s strategy is “synchronized with the government,” he said.
Value Assessment Vexes Pharma As China Costs Soar, Prices Fall

**Executive Summary**
Traditionally a low-cost manufacturing haven, China has seen pharma R&D costs increase rapidly although prices for pharmaceuticals have not gone up, forcing officials and executives to explore value assessment and market access approaches in a toughening environment.

Jiangsu Hengrui Medicine Co. Ltd. is widely considered a national champion for the pharma industry in China, having not only licensed an anticancer asset to US firm Incyte Corp. in a $900m deal, but also developed its own oncology drugs that have gained several approvals in China.

In the first quarter, Hengrui reported its revenues jumped by 29% to CNY4.97bn ($719m), driven by new launches including anticancer drug Iruini (pyrotinib), and another oncology product, apatinib, that was launched earlier.

On the other hand, the Lianyungang-based company also reported that R&D expenses grew even faster than sales, up 57% compared to the same period in 2018; its quarterly R&D costs reached CNY662m.

This relative level of R&D spending (equivalent to around 13% of sales) puts Hengrui in the same league as its overseas peers, the only issue being that it can't command the same price premiums for novel new drugs as these companies, noted Jianjun Zou, a vice-president at the company.

“Our R&D expenses are on a par with large drug makers but the product price in China, for instance, is like CNY200 [$30] compared to $1,000 in the US,” Zou told attendees at the Drug Information Association’s China annual meeting, held 22-24 May in Beijing.

Zou’s reference to the large price gap reflects a widening view that China’s price control policies, including steep price reductions in exchange for reimbursement coverage, could potentially deter innovation in the sector.

Assessing a novel drug’s proper valuation is thus seen as key in pricing policy and negotiations, especially during this time when China is building up to including many additional new drugs in its National Drug Reimbursement List (NDRL), a process that started this April and will be complete in September. Any products that have been approved in the country prior to 1 January are eligible for the coverage.

The process is divided into two stages, one for low-priced drugs that will be added without pricing negotiations and another for high-priced products, for which many are expected to go through multiple rounds of pricing negotiations.

Out of 17 anticancer drugs that were covered using a similar mechanism in the past, the average price reduction was 55%.

**R&D Cost Consideration**
Entering May, China is kicking into high gear for the NDRL update and drug companies are busy persuading medical experts about the value of their products.

Doing so needs a large amount of epidemiology data which needs to be assessed with a holistic view, Kun Zhao, director of Health Technology...
Assessment (HTA) at the China National Health Development Research Center, told the DIA meeting.

Real world evidence, and not only data from clinical trials, is playing a growing role in determining product value, noted Zhao, while citing uncertainties in these studies. “Is it an iceberg or just the tip?” he asked.

Furthermore, a clear mechanism and transparent process are needed, so guidelines and methodology should be publicized to convince the public, stressed the expert. For drug makers like Hengrui, experts should take R&D costs into consideration in order to provide a fair assessment, Hengrui’s Zou said.

Market Access Issues
Aside from such assessments, market access also poses a major challenge for high-priced drugs in China, including the world’s best-selling biologics. AbbVie Inc.’s Humira (adalimumab) may have $20bn in worldwide sales but just $20m - 0.1% of this figure - in China, noted Ning Li, CEO of Junshi Pharmaceutical Group.

“There is more that can be done besides quantifying a product’s value using HTA analysis, especially when it comes to drug pricing,” Li proposed during a panel discussion at the annual gathering. Such options include patient assistance programs (PAPs) and local provincial reimbursement schemes.

Li’s company is one of four makers of immunooncology products that have been launched in China, where its Tuoyi (toripalimab) became the first domestic IO agent to be approved. However, it is priced at CNY7,200 per 240mg vial, less than half the level of Merck & Co. Inc.’s Keytruda (pembrolizumab), which costs CNY17,918 per 100mg in China. This in turn is already nearly 50% lower than the drug’s US price.

Better Positioning
Pricing aside, both domestic and foreign drug firms routinely provide PAPs to qualified patients in China, with Merck and Junshi having such schemes in place that award free drugs after a certain amount of purchases.

Pricing, PAP and private insurance are known as the “three Ps” for both multinational and innovative domestic companies wanting to expand product access in China.

Despite the national reimbursement scheme offering potentially large volume uptake, companies are also now actively looking to get local coverage that will help new drugs get to patients faster. Both Keytruda and Tuoyi, for example, were recently added to Zhuhai city’s coverage scheme for cancer treatments. This means a patient can get 90% of the cost covered for the purchase of listed anticancer drugs priced in a range of CNY10,000 to CNY300,000.

The combination of pricing strategy, local scheme coverage and PAPs will hopefully provide buffers for pharma companies to feel better positioned entering negotiations for NDRL coverage, or some might even forgo the process altogether.
How To Deliver Your China Growth Story: Trends To Watch

Executive Summary
Caught between a grueling centralized bidding process and now potentially in trade war crossfire, foreign pharma firms have a lot on their plates in China. To succeed in this highly uncertain environment, observers point to the need to pursue excellence in multiple areas: product launches, medical coverage, the broad market and digital health.

Barely a day goes by without major developments coming out from China, and an escalating trade dispute with the US and a slowing domestic economy are among the most recent headlines. For the pharma sector, the rapid roll-out of a massive centralized bidding scheme in major cities is adding to the growing list of operating uncertainties.

Although pharma companies have so far largely avoided the impact of the brewing trade war between the world's two largest economies, China has vowed to retaliate with more tariffs. China imports finished drugs and medical devices from the US, and although medicines are far below aircraft and large machinery in total monetary value, some worry that the higher tariffs could expand to such products.

In the past, the Chinese government has actually lowered import tariffs for imported anticancer drugs, in a bid to make them more affordable to local patients.

Meanwhile, in the first three months of 2019, China continued to deliver as a growth engine for the multinational pharma industry, providing north of 20% growth for several firms including AstraZeneca PLC, Pfizer Inc. and Sanofi. Merck & Co. Inc. reported its sales in the country rose by a jaw-dropping 66% in the period.

Several underlying factors contributed to the strong growth, including increased uptake of new products, but there are looming challenges, the biggest of which is the “4+7” centralized procurement scheme for 11 major cities. (Also see “Drug Price Waterloo: China’s New Bidding Process Hits MNCs Hard” - Scrip, 11 Dec, 2018.)

Against this fast-developing background, there are several needs and trends in China that pharma companies should pay close attention to, local analysts say.

New Product Launches
Amid China’s positive regulatory reforms and higher numbers of new drugs gaining approvals, companies need to have a multi-channel strategy to generate the most “bang for the buck.”

“A lot of these [strong Q1 growth rates] were driven by newly launched innovative products, as a result of expedited regulatory processes to get products registered in China,” Justin Wang, a partner at consulting firm L.E.K.’s Shanghai office, told Scrip. Such products included AZ’s Tagrisso (osimertinib) for lung cancer, and Merck’s HPV vaccine Gardasil and PD-1 inhibitor Keytruda (pembrolizumab).

“These new products are able to address significant unmet clinical needs and have been long expected by the China market. Successful market education, as well as additional patient assistance programs, are also driving the rapid uptake,” Wang noted.

Oncology and vaccines are two areas that have seen significant growth in China in recent years.
The new generation of immuno-oncology agents has also gained the spotlight and generated excitement in China, where cancer incidence and mortality rates are steadily increasing.

According to the China National Cancer Center’s most recent data, 3.9 million people were diagnosed with cancer in the country in 2015, when there were 2.3 million deaths.

Access Issues
Given there is no immediate or automatic insurance coverage for new drugs in China, companies may need to craft patient assistance programs that enable expanded access and are also able to accumulate actual clinical use data following launch. These can take the form of provision of product or other effective subsidies to out-of-pocket costs.

But seeking reimbursement remains an important potential catalyst for sustaining growth. In 2019, China’s Medical Insurance and Support Administration will expand the National Reimbursement Drug List (NRDL) to include selected drugs approved before 31 December 2018. For high-priced products, such inclusion will only come along with price negotiations, which in a previous case for 17 anticancer drugs led to prices being slashed by an average of 57%.

While NRDL coverage provides potential volume gains, the associated price reductions may also prompt manufacturers to weigh the risk of rapid and substantial price erosion. “Most MNC pharmas will certainly prioritize NRDL listing for their market access efforts, but there is certainly a subset of international pharmas that would prefer to stick to their global pricing band,” said L.E.K.’s Wang.

During Merck’s quarterly earnings call, chief commercial officer Frank Clyburn noted that while the US firm hopes to have its newer products such as Gardasil, Keytruda and others covered by the list, strong market positioning was still possible without this. “A listing would open up an exciting opportunity to expand volumes. But even without that, we feel that we’re very well positioned for Keytruda in China with the only PD-1 that has a first-line lung cancer indication,” he commented.

Broad Market, Digital Health
Another important potential growth area for multinationals in China is the so-called “broad market” of smaller but still sizable cities, which has traditionally been defined as tier 3 cities but now extends down to tier 4 and 5 cities.

“Many also say that multinationals were able [in the first quarter] to exploit opportunities from new channels (eg, lower-tier cities, retail and direct-to-patient) that offset volume declines in their core markets,” said L.E.K.’s Wang.

Known for being particularly price-sensitive, the lower-tier market will be hard for many to crack. To that end, many foreign companies are increasingly integrating digital technology into their commercial strategy, for products ranging from HPV vaccines to consumer health brands.

The latest example involves GlaxoSmithKline PLC and AliHealth, which on 2 April signed a joint business plan covering big data, and new sales models and services. Consumers will receive online information on respiratory and pain management products, plus web-based medical consultation and education, the aim being to improve medication awareness.

Novartis AG on 22 March also signed on with major Chinese e-commerce group Tencent to use artificial intelligence technology to provide heart failure solutions. The agreement is expanded on previous agreement on chronic diseases management.
Other multinationals including Merck KGaA and Pfizer are also getting aboard the digital health train in China. (Also see “Merck KGaA, Pfizer Dance To China Digital Health Beat“ - Scrip, 29 Jan, 2019.)
Calm Before The Storm: Pharma Opens 2019 With A Bang In China

Executive Summary
Products old, new and reimbursed were the driving force for foreign drug firms including AstraZeneca, Merck and Pfizer and Sanofi to smash growth in China in the first quarter.

Pharma multinationals have started off strong in China in the first quarter, helped by growth for both mature and newer products, but several are also issuing cautions that there may be a general slowing in growth amid broader changes in the economy. A new competitive bidding scheme in major cities in particular is expected to put considerable further pricing pressures on some companies and products.

AZ’s $1bn Quarter In China
Pointing to a historical high growth rate in emerging markets in the first quarter, AstraZeneca PLC said this was being driven by China, which soared by 28%, but also a strong showing across all such markets globally.

The UK-based company’s overall EM sales broke the $2bn mark, with more than $1bn coming from China for the quarter. This was driven mainly by oncology star Tagrisso (osimertinib), which in emerging markets delivered $138m, with China contributing more than half of this after being included in the national reimbursement drug list.

But the tide may be changing. “We want to flag that we expect China to still continue growing at a fast clip but not as fast as we have experienced lately because we will start being impacted, as other companies, by the changes in the marketplace,” cautioned CEO Pascal Soriot during a 26 April earnings call with investors.

The biggest market change in China is the so-called “4+7” centralized procurement scheme, a massive tendering process that is being rolled out in 11 major cities and is expected to significantly slash drug prices, and in one extreme example has led to a 96% reduction.

AZ’s Crestor (rosuvastatin) and Iressa (gefitinib) were both selected in the first round of bidding, but while Iressa won, Crestor lost out to a domestic maker. “In the second half [it] will be Crestor because we lost a tender...so certainly, that product will be impacted,” Soriot noted.

When asked about a recent report that China and the US have agreed to set the data exclusivity time frame for biologics at eight years in China, the CEO considered it progress instead of detriment. “I think the fact that we are debating eight years or 10 years or more is actually reflecting that there is a discussion around IP [intellectual property] rights [in China], which is a good discussion to have.”

Pfizer Sees Headwinds Ahead
Pfizer Inc.’s first quarter earnings in China show that established products continued to grow nicely. The US drug maker, which has a separate established products unit, Upjohn, said overall business revenues in the country grew 1% operationally in the quarter.

“We believe Upjohn will help us seize the tremendous opportunity we see in the emerging markets,” noted company chief financial officer Frank D’Amelio during Pfizer’s 30 April quarterly results call with investors.

“As the global middle-class continues to rapidly expand, and as awareness and diagnosis and
treatment options continue to improve, we believe the Pharmaceutical segment will continue to enjoy significant expansion in Greater China and other emerging markets.”

Upjohn is managing 20 products in 65 markets with its leadership located in China, where the government has vowed to up efforts to drive generics and biosimilar approvals and manufacturing.

Mature products with growth in China singled out by the executive were largely cardio-vasculars, namely Lipitor (atorvastatin), Norvasc (amlodipine) plus Celebrex (celecoxib).

Despite the growth, the company also said headwinds are coming and that a bumpy ride is in store. The 4+7 bulk procurement scheme is expected to negatively impact drug makers with a large established products portfolio.

“Our guidance continues to reflect expected headwinds in China due to pricing reform, which is now being implemented,” said the CFO. Pfizer did not win the bids for Norvasc and Lipitor in the 4+7 bidding process due to their relatively high prices.

Although novel products are expected to offset some of the losses, given that there is no immediate reimbursement for newly launched drugs in China, there will be time delays, analysts say.

Novo Sees 90% Growth For Victoza
Danish diabetes specialist Novo Nordisk AS saw Q1 China sales increase by 9% at constant exchange rates, driven by its insulin preparations and GLP-1 products, for which sales rose 9% and 90% respectively.

The company benefited from high market growth in long-acting basal insulins and fast-acting insulin lispro. Riding the wave, Novo’s pre-mixed insulins sales grew by 10% in the quarter, although human insulin were down by 3%.

Novo’s latest addition to its product mix in China, the GLP-1 agonist Victoza (liraglutide), reported 90% growth in the three months, showing the strong demand for newer anti-diabetes treatments in China.

Merck & Co ‘Only Scratching Surface’
Emerging markets also represent a large growth opportunity for Merck & Co. Inc., but so far the US company is only just getting started, said CEO Ken Frasier.

“We believe that we’ve only scratched the surface in terms of the opportunity in key markets such as China, where we are seeing significant growth,” noted the CEO on the 30 April earnings call.

Overall, Merck growth was strong in both the US and international markets in the quarter, but especially in China, where sales soared 67% year-over-year, driven largely by newly launched products such as human papillomavirus vaccine Gardasil and immuno-oncology agent Keytruda (pembrolizumab), among others.

The local demand for the HPV vaccines is such that many clinics are running out of stocks, prompting Merck to reevaluate and rearrange supplies. Keytruda’s recent approval for first-line for non-small cell lung cancer also give an additional boost to the company. (Also see “China Appetite For HPV Vaccine Delivers Surprise For Merck” - Scrip, 2 Aug, 2018.)

Given what it sees as a good outlook in China for two other new oncology products, Lynparza (olaparib) in collaboration with AZ and Lenvima (lenvatinib) with Eisai Co. Ltd., the company is feeling rosy about its prospects in this market.
China has initiated a medical reimbursement policy that aims to cover more and newer oncology and rare disease treatments, and Merck executives say they are on board. (Also see “Cancer, Rare Disease Drugs To Be Covered As China Expands Reimbursement” - Scrip, 15 Mar, 2019.)

“We will be working through the NRDL [national reimbursement drug list] listing process with the Chinese regulators. And given the timing of our lung cancer approval, we'll have to see if NRDL listing is a possibility this year,” Frasier said.

The reimbursement qualification requires products to have been approved on or before 31 December 2018, putting Keytruda - which gained its first approval in China in 2018 for melanoma and then the NSCLC indication this March - in an unpredictable situation.

“A listing [on the NRDL] would open up an exciting opportunity to expand volumes. But even without that, we feel that we're very well positioned with Keytruda in China with the only PD-1 that has a first-line lung cancer indication,” noted chief commercial officer Frank Clyburn.

He also pointed to the breadth of the development program for the molecule, as seen in other markets, noting “We plan to bring additional indications to China, which we think positions us very well for future growth.”

Q1 Strongest For Sanofi?
China remains a key driver for French group Sanofi, which saw broad-based growth of 22% in China in the quarter, driven partially by its pediatric vaccines, whose sales grew by 26%, with the five-in-one vaccine Pentaxim particularly strong.

However, the company also cautioned that the 4+7 scheme is expected to affect company revenues in China over the rest of the year.

“Looking ahead [the new scheme] is expected to result in lower growth rates for Plavix [clopidogrel] and Aprovel [irbesartan] for the full year of 2019. As a result, the first quarter performance will likely be the strongest quarter of the year for China,” noted CEO Olivier Brandicourt in the 26 April quarterly earnings call.

Sanofi’s head of emerging markets and China, Olivier Charmeil, pointed out that roughly one third of its business in China will be impacted by the centralized bidding program.

“So how will we look at it at the end of the year, given the new volume-based procurement system is going to impact Aprovel and Plavix in roughly 30% of the total market? So we are still expecting overall good growth for 2019, but it's likely, as Olivier alluded to, that the first quarter performance will be the strongest in the year,” Brandicourt said.
**Executive Summary**

Facing unprecedented pricing pressures in China, multinationals are embarking on a major shift away from mature products to focus more on innovative drugs, but there are major challenges linked to the transition that won’t be easy to navigate, notes a new report.

After years of pondering, now comes concrete action.

Amid unprecedented pricing pressures in China, pharma multinationals operating in the country are transitioning to focus more on innovative new drugs rather than relying on their traditional cash cows of branded but off-patent products.

Eli Lilly & Co. has become the latest to divest selected established products to a domestic drug firm in China, to help focus resources on new therapies. The US major announced an agreement with China’s Eddingpharm International Holdings Ltd. worth $375m, under which it is handing over exclusive local marketing rights to two antibiotics, Vancocin (vancomycin) and Ceclor (cefaclor) in mainland China.

Furthermore, Lilly will also sell off its cefaclor manufacturing site in Suzhou, Jiangsu Province to the Chinese company. (Also see “Asia Deal Watch: Shionogi Finds Commercial Partners For Symproic In US, Europe” - Scrip, 23 Apr, 2019.)

It’s the second time in six months that Lilly has been in the spotlight for such moves. The US drug maker in late November was reported to be looking for potential buyers for multiple products in China including its best-selling CNS drugs Zyprexa (olanzapine) and Prozac (fluoxetine), among others. The sales value of the portfolio to be divested was said to be $200-300m. (Also see “Multinationals Eye Divesting Established Products In China Amid Fierce Competition, Shifting Focus” - Scrip, 25 Nov, 2018.)

Divestments of established products aside, Lilly has also been in several collaborations with domestic innovative pharma companies in China, including Innovent Biologics Inc. and Hutchison MediPharma Ltd. (Chi-Med). So far, Innovent’s PD-1 checkpoint inhibitor sintilimab and Chi-Med’s fruquintinib have gained approvals in China.

Lilly has also been moving to establish collaborations for diabetes physician and patient education with Chinese digital health player DXY and the company’s controlling stakeholder Tencent.

**Divesting Non-Core Assets**

Lilly is just the latest multinational to divest established assets to Chinese domestic firms, and the trend is likely to continue. But the ongoing transition away from mature products and refocus on innovative new drugs is littered with challenges, noted a recent report by global consultancy Ernest & Young (EY).

Similar divestments have been taking place at other MNCs operating in China. Roche in 2018 sold its anemia treatment Recomon (recombinant human erythropoietin β injection) to Eddingpharm, one year after it was included in China’s national reimbursement list.

Months later, the Swiss group divested the antiviral for hepatitis B and C Pegasys (peginterferon alfa-2a) to Hangzhou-based Ascletis Pharma Inc., which will market it in China.
The divestment came as part of Roche’s strengthening focus on its core areas, notably oncology. The company in early 2018 also initiated a reorganization of its China operations, establishing two business units devoted to cancer products, on top of a specialty medicines unit and a primary care unit.

Driven by the renewed focus, Roche has seen some initial results including growth for its anticancer franchise, comprising both targeted therapies and biologics, as well as growth for newer products for hemophilia and multiple sclerosis.

**Spinning Off**

In effect, international pharma companies including AstraZeneca PLC have been actively looking to offload in China some best-selling products whose patents have expired, in a move to concentrate more in this market on innovative drugs that have recently gained approval.

The UK-based firm sold its best-selling Seroquel (quetiapine) franchise to Luye Pharma Group Ltd. in May in a deal worth $546m, in an agreement giving Luye marketing rights to the CNS drug in 51 designated countries.

This January, AZ then obtained exclusive rights to market Luye’s Xuezhikang natural product-derived, lipid-regulating capsules in mainland China, a deal that allowed the UK firm to maintain its presence in the country’s cardiovascular market amid price pressure on its blockbuster Crestor (atorvastatin), stemming largely from the roll-out of the “4+7” national centralized bidding scheme in 11 major cities. (Also see “Drug Price Waterloo: China’s New Bidding Process Hits MNCs Hard” - Scrip, 11 Dec, 2018.)

For US firm Pfizer Inc., its transition in China has meant spinning off its established products to its Upjohn Laboratories subsidiary. (Upjohn became a part of Pfizer when Pfizer acquired Pharmacia in 2002.)

Several best-selling Pfizer cardiovascular treatments are now part of the Upjohn portfolio, including Lipitor (atorvastatin), Norvasc (amlodipine) and Celebrex (celecoxib). The spin-off is expected to focus on life cycle management while Pfizer will focus on innovative new products.

**More Challenges**

The 4+7 scheme is expected to give domestic drug makers with lower-priced products an opportunity to compete directly with MNC products, and to bring down prices to a level never seen before.

The EY report, released April 19 and titled MNCs’ Strategy to Cope With New Health Reforms, details four major challenges facing multinationals in China. A major one cited by the global consultancy is heating up competition from domestic generics firms, given that 60 such operations have now cleared bioequivalence testing, equating to 80% of total sales.

Other challenges identified by EY include: innovative pipelines lagging the regulatory approval and reimbursement cycles; a need for rapid ramp-up in marketing and promotional capabilities given more new drug approvals; and a need for improved sales efficiency.

As the Chinese government steps up drug price controls, there would appear to be little room for negotiation, and manufacturers eyeing trading price reductions for market share need to improve efficiency to lower operational costs, noted the EY report.

**Innovation Alone Not Enough**

Although multinationals are hoping to make up the lost revenues from product divestments in
China with increased uptake of innovative drugs, the rate of this replacement may not be fast enough. In addition to the rapid launch of new drugs, foreign firms need to improve market access schemes, and work to get insurance coverage of their products.

China is also considering a new round of revisions to the National Reimbursement Drug List revision, which will take place throughout the year, and producers should actively take part in the process. Additionally, they should explore inroads into China’s “broad market” comprising tier 3, 4 and 5 smaller urban and county-level cities and hospitals, EY suggests.

“Although for MNCs, they won’t be able to enjoy a price premium for their off-patented products, several innovation-oriented policies provide some opportunities for them in much broader market segments. MNCs meanwhile have to pay attention to mitigate risks during the transition, and fully prepare for it,” advised Helen Wang, EY’s managing partner for the consulting business.
Merck KGaA, Pfizer Dance To China Digital Health Beat

Executive Summary
Facing deep price erosion and fierce competition for their established products, more multinational firms are hopping on the digital health train in China, with Merck KGaA and Pfizer becoming the latest to tie up with the country’s internet giants Tencent and AliHealth, respectively.

More foreign pharma companies continue to enter the digital health sector in China, including Pfizer Inc., which has signed a new memorandum of strategic cooperation with Alibaba’s health subsidiary Alihealth to cooperate on digital technology for drug traceability, smart healthcare and physician education.

The agreement marks an expansion of a previous deal between the two companies signed in March 2018, which focused mainly on drug safety.

The new partnership with Alihealth will allow Pfizer to provide online physician training, including inviting medical experts in various disease fields in China to use the Mayo Clinic education system, and materials introduced by Pfizer, to provide systematic professional academic courses with a focus on pediatric, male reproductive, pain management and cardiovascular conditions.

The move comes against the background of the roll out by the Chinese government of tiered healthcare services, which is forcing more drug makers to expand their reach beyond traditional 3A (top class) hospitals, mega-cities and tier 2 to broader lower regional hubs and county-level medical facilities. Major MNCs are also facing more competition from domestic firms and slowing growth in China for some of their key products.

To better reach the large number of China’s grassroots hospitals, multinationals are increasingly making use of mobile and digital tools, usually via partnerships with the country’s three internet giants - Baidu, Alibaba and Tencent, collectively known as BAT.

The tiered care system requires patients to receive their primary care and diagnosis from local health facilities, making these an increasingly important target for pharma firms.

In addition, the new “4+7” drug supply bidding mechanism for commonly used products initiated at 11 cities around the nation means that foreign companies are preparing for further price erosion for their off-patent originator products, again making broader outreach increasingly important.

Merck KGaA’s Chronic Disease, Oncology Push
So called “internet+ healthcare” is marching on in China, and more foreign drug makers are now embracing it with open arms. Digital health and artificial intelligence is one of nine major trends for the biopharma commercial in China this year predicted by the Scrip.

Along these lines, Merck KGAA on Jan. 23 picked Tencent as a partner and teamed up with the Shenzhen-based tech giant to raise public awareness of certain diseases, and to provide more accessible medical services in China through digital platforms.

The two partners will develop smart digital healthcare services to improve patients’ understanding of symptoms and availability of treatment options. The alliance will aim to bring more convenient medical services to patients to
help them with chronic disease management, the firms said.

Other MNCs including AstraZeneca PLC, Merck & Co. Inc. and Sanofi have already partnered with AliHealth for various digital health services, while Tencent runs China's most popular social networking tools such as Weibo and Wechat, which both have tens of millions of active daily users.

In 2018, Tencent underwent a major shift from the C (consumer) to the B (business) sector, and made healthcare services one of its prioritized areas of focus.

Merck KGaA meanwhile has a strategic interest in chronic diseases, and the German company hopes the new tie-up with Tencent will enable it to explore digital services aimed at raising awareness of allergic disorders and improve treatment compliance for allergy sufferers.

In the area of assisted fertility, the partnership will begin to raise awareness of disorders and treatment options, and help people in need shorten their access to medical procedures. The two sides will also work together on diabetes, thyroid and cardiovascular diseases, as well as in metastatic colorectal cancer, where Merck has a presence through Erbitux (cetuximab).

Looking ahead, the partners also plan to explore innovative medical service models based on artificial intelligence, to provide more comprehensive disease science and services both in the field of metastatic colorectal cancer and other diseases.
Drug Price Waterloo: China’s New Bidding Process Hits MNCs Hard

Executive Summary
China’s new so-called “4+7” drug bidding pilot scheme, already expected to be a killer for some companies, has cut prices by as much as 90%, leaving all but two multinationals to bid successfully and accept the revised levels. The big reductions could also lead to further price erosion for the winning products.

The results of a new pilot drug price bidding scheme, announced by China’s new Medical Insurance and Support Administration (MISA), sent immediate shock waves to the market, leading to instant trading halts for many publicly traded drug makers in Shanghai and Shenzhen as they were affected by the process.

Although the “winner takes all” model of highly centralized product bidding, the first ever for China, affected both domestic and international companies, underlined by a broad decline in shares prices, multinationals seemed to bear the brunt of the likely commercial hit.

The so-called “4+7” bidding scheme is named for the number of cities picked for the pilot, which will start in the four top-tier conurbations of Beijing, Tianjin, Shanghai and Chongqing, plus the seven second-tier urban centers of Shenyang, Dalian, Xiamen, Guangzhou, Shenzhen, Chengdu and Xi’an.

Under the scheme, a Joint Procurement Office bids for the supply of products at the lowest price on behalf of public hospitals in their areas.

One of the main reasons for the pilot, noted the MISA in its announcement, is that the regulators believe the effect of the “patent cliff” for some major older products has still not been realized in China, meaning that some off-patented originators drugs continue to command a price premium in the country.

Cuts Range Up To 96%
The results announced Dec. 6 show that the 31 selected drugs for the scheme include some widely-prescribed treatments such as AstraZeneca PLC’s Crestor (rosuvastatin), Pfizer Inc.’s Lipitor (atorvastatin), and Norvasc (amlodipine), and other best-selling cardiovascualrs including Merck & Co. Inc.’s Cozaar (losartan) and Sanofi’s Plavix (clopidogrel), but also the CNS drug Johnson & Johnson’s Risperdal (risperidone) and Bristol-Myers Squibb Co.’s Baraclude (entecavir).

Additionally, some commonly used anticancer drugs including Novartis AG’s Gleevec (imatinib), AstraZeneca’s Iressa (gefitinib) and Eli Lilly & Co.’s Alimta (pemetrexed) were also included in the bidding list.

Out of the total, the price bids for 25 drugs have been accepted, meaning an 81% success rate but leaving nearly 20% still to be decided.

“The average price reduction is 52% and the steepest cut is 96%, reflecting a significant reduction,” noted the MISA in its statement. “[The off-patented products’ prices] are now 25% lower than the average reference prices of surrounding markets, showing the effect of the ‘patent cliff,’” added the agency.

What’s most notable in the process is the large number of multinationals to have lost bids, with only two MNCs successfully winning these, one being AstraZeneca with Iressa and the other BMS
for Monopril (fosinopril). As part of the bidding scheme, however, AstraZeneca agreed to lower the price of Iressa by 76% while BMS cut its Monopril price by 68% in order to get into the game, which promises increased volumes.

Winners of the bid win the right to supply the product to the cities at the agreed price for one year, and to provide additional quantities at the same price if the original quantity is used up before this time.

**Price Watershed?**
But industry observers quickly pointed to a nosedive in prices for some best-selling generics that won this bidding round. One of these was amlodipine, for which branded Norvasc has seen dozens of competitors. Amlodipine tablets from a relative newcomer, Zhejing Jingxin Pharma, won the bidding this time at a price of CNY0.14 ($0.02) per tablet, roughly 97% below Norvasc’s listed price of CNY5.

“Dec.6 marks the beginning of China’s generics market to be taken over by [low-priced] generics, and the end of two eras, one when generics are high-priced, having high-profits and high promotion fees, and another era when branded generics dominated with large market shares,” CEO of Chinese drug maker Canion Pharma Wu Jiqiang predicted in an interview with local media E-Pharma Managers.

Representatives from research-based multinational drug makers have already expressed opposition to the pilot scheme. Jean-Christophe Pointeau, president of the R&D-based Pharmaceutical Association Committee (RDPAC), a major industry trade group representing 40 firms in China, said “it’s not a right move”, adding that “people can lower drug manufacturing costs, but it should not be at the expense of drug quality.” The executive is the president of Sanofi Pharma China.

Addressing the quality concerns, MISA said that all 22 bid-winning drugs made by domestic firms had cleared bioequivalence testing, showing that their quality is equal to the off-patent reference products.

**Ripple Effect?**
Despite the increase in expected volume uptake for the bid-winning products, which could partly offset lower prices, the unusually deep erosion of drug prices in the process has many worrying about a domino effect on the pharma sector.

The real impact, analysts say, could come from a ripple effect created by the sometimes shockingly steep price cuts, and the winning bid prices could be used as a reference for other products during future rounds of bidding.

“The volume [reported by each 4+7 city] may not reflect the real demand, but the prices could still be used for follow-on purchases,” commented Yang Song, an analyst at Guotai Junan Securities. Shanghai, for one, has issued complementary policies to the bid that require hospitals prioritize to use the winning products, and other cities may soon follow its lead, noted the analyst.

**Looking Forward**
However, MISA said in its statement that the market selloff and strong reactions to the deep price reductions are an over-reaction, stressing what it sees as the transparency and fairness of the process.

“Drug price inflation has long been an issue,” said the agency. “The price reduction is only a move to squeeze out inflation, and drug makers can still make a profit.”

Facing fierce competition and mounting price pressures, many multinationals operating in China are now largely shunning branded generics, and are instead turning their focus to innovative new
drugs that will offer better pricing power. (Also see “Multinationals Eye Divestings Established Products In China Amid Fierce Competition, Shifting Focus” - Scrip, 25 Nov, 2018.).

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