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MSD's Asia Pacific Chief On Lagevrio's Gains In Clinical Utility Amid Paxlovid Luster

by Anju Ghangurde

David Peacock, President, Asia Pacific, MSD tells Scrip how Lagevrio has gained dominance in certain parts of the world, though Paxlovid may have received the 'lion's share' of public attention.

Pfizer Inc.'s Paxlovid (nirmatrelvir/ritonavir) may be in the spotlight as the star antiviral for COVID-19 but beyond the headlines *Merck & Co., Inc.*'s Lagevrio (molnupiravir) is making strong headway, at least in some parts of the world and there's more to come, a senior executive of the company has indicated.

David Peacock, President, Asia Pacific, MSD, as Merck is known outside the US and Canada, noted that while Paxlovid has received the "lion's share" of public attention, a lot probably comes down to its first clinical data set that were shared with the world, which at the time, were seen to be superior to Lagevrio's initial results. (Also see "*Pfizer's Oral COVID-19 Pill Paxlovid Tops Merck's Molnupiravir*" - Scrip, 5 Nov, 2021.)

"However, in the actual clinical utility, the story is actually quite different. In different parts of the world, Lagevrio is actually 'dominant'. This is true in much of Asia Pacific, whether that be Japan, Hong Kong, Australia - a lot of that comes down to clinical practice," Peacock said in an interview with *Scrip*.

He explained that the population being treated often tend to be at higher risk, and therefore are likely to be on multiple medications. Lagevrio, developed with *Ridgeback Biotherapeutics LP*, does not have significant drug-drug interactions unlike ritonavir, a key component of Paxlovid, that comes with certain restrictions. (Also see "*Merck/Ridgeback's Lagevrio Could Get Another Chance As Others Face Limitations*" - Scrip, 1 Apr, 2022.) (Also see "*Could Pharmacist Prescribing Grow In Wake Of Paxlovid Experience?*" - Pink Sheet, 7 Jul, 2022.)

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“So there will be an enormous need,” Peacock, who has held leadership roles at the US company including as MSD managing director in the UK and Ireland, predicted.

Paxlovid’s drug-drug interactions and renal impairment adjustments are some of the key treatment challenges, though Lagevrio too comes with risks of embryo-fetal toxicity (based on pre-clinical evidence) and impacts bone and cartilage growth but those are not seen as huge concerns for the elderly, who are at high risk of COVID-19 complications.

‘The World Needed Actual Supply’

Lagevrio recently hit a milestone, with over one million patients globally having received the antiviral. That doesn’t include molnupiravir versions available via the non-exclusive voluntary licensing agreements with leading Indian generic manufacturers including *Sun Pharmaceutical Industries Ltd.*, *Dr. Reddy's Laboratories Ltd.* and *Cipla Limited* or the licensing agreement with the Medicines Patent Pool (MPP) to expand access for molnupiravir in 105 low- and middle-income countries (LMIC) following regulatory approval. (Also see "*Molnupiravir India Licenses: Nuances, Local Data In Focus*" - Scrip, 28 Apr, 2021.) (Also see "*Merck’s Molnupiravir Open License With Medicines Patent Pool May Be Model*" - Pink Sheet, 27 Oct, 2021.)

On suggestions in some legal and other quarters that the voluntary licensing deals were driven, in part, to avoid high decibel patent litigation/ compulsory licensing efforts amid a raging pandemic, Peacock said that at the end of the day, what "the world needed was actual supply"; academic arguments need to be “put to the side” in the midst of a crisis, he reasoned. (Also see "*Pharma’s Voluntary Licensing In India Successful In 2021 – But There Were Some Delicate Moments*" - Pink Sheet, 6 Jan, 2022.)

WTO IP Waiver ‘A Step Backwards’

David Peacock, president (Asia Pacific), MSD, doesn’t believe that the World Trade Organization’s decision on an intellectual property (IP) waiver for COVID-19 vaccines is the real solution to the pressing problem to rapidly expand access to inoculation.

The executive laid out that first the world needs to recognize that COVID-19 vaccines and the therapeutics that have been developed are results of years of research.

“There's a common misperception that these vaccines and treatments were begun when the pandemic started, and it's complete fallacy. People have been investing decades into the technologies both at the molecular level as well as the production level that enabled us to respond as an industry as effectively as we have,” he explained.

Peacock underscored that IP needs to be protected to enable companies like Merck and the broader scientific community, universities etc. to be able to battle the next set of crises when they emerge.

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"This is not something to be solved in a courtroom but something to be solved in a manufacturing plant. People may argue that we were protecting certain markets from broader supply, etc - that's an understandable consequence. But that's why we leveraged our own internal capacity," he explained.

The company focused its efforts on those markets that "we knew had the capability to pay", and ultimately would be getting a cost-effective price.

"It's not that we were setting monopolistic prices... we engaged with all these regulators the same way we do with all of our products, and they pay the price that they believe is fair, " he added.

Drug-Drug Interaction - A Primary Concern

While some of Lagevrio's dominance in certain regions of the world may, in part, be due to the slow ramp up in terms of supply availability of Paxlovid, Peacock reiterated that that "a lot of it" really comes down to the clinical utilization.

"You're really looking at treating patients in aged care facilities in homes where drug-drug interaction is of a primary concern and so, physicians and pharmacists kind of tend to steer away from ritonavir- boosted medicines". (Also see "*Pfizer's Paxlovid Likely Relegated To High-Risk COVID-19 Patients*" - Scrip, 15 Jun, 2022.)

"I really think the waiver is an enormous step backwards. I think it is a proposed solution but the wrong solution to a real problem."

The problem, he defined, is that there are a number of places in the world that still struggle to gain access to vaccines in enough supply. The core issue lies in the "inefficiency" of multilateral systems to push the supply.

"It's not even an affordability question, because the donation programs etc. have made the doses available. It literally is a problem getting the drugs from point A to B. IP is not an issue. These are issues of logistics, and in some cases, manufacturing," he maintained.

When companies such as Merck recognize these challenges they enter into arrangements like voluntary licensing or the MPP partnership, though for vaccines, things are a little more complicated, especially when you're talking about some of the new brand new technologies, he explained.

"But once again, it's not an IP issue. Even if you had open IP, a manufacturer in South Africa may not have the technical know-how to be able to manufacture. So what have you done other than weaken the incentive for the originator to invent?," he asked. (Also see "*Afrigen Chief On mRNA Vaccine Candidate, IP Hoops, Market-Shaping Efforts*" - Scrip, 25 Feb, 2022.)

While Lagevrio and Paxlovid are currently authorized for emergency use, with the clinical community still working to figure out exactly

how broadly they be should utilized, things appear to be changing as physicians gain experience.

"We saw that recently, where the Australian government is moving forward with plans to expand access - they opened the aperture in terms of which population can gain access, and once again that's built off the back of successful utilization," Peacock explained.

Australia recently widened eligibility for the antiviral treatments permitting, from 11 July, all Australians aged over 70 who test positive for COVID-19 to access these treatments on the Pharmaceutical Benefits Scheme. Access has also been expanded to those over 50 with two or more risk factors for severe disease, Aboriginal or Torres Strait Islander people aged over 30 with two or more risk factors for severe disease. Immunocompromised people over 18 may also be eligible.

He believes the WTO actions were more an issue of "politics over pragmatism".

"The issues persist, even with this waiver. I don't believe that sharing open IP is actually going to solve the issues. It comes down to logistics, and manufacturing, and that can be done through existing mechanisms."

WTO members had, at the 12th Ministerial Conference which concluded in Geneva on 17 June, endorsed authorizing the use of the 'subject matter' of a patent required for the production and supply of COVID-19 vaccines without the consent of the right holder to the extent necessary to address the COVID-19 pandemic, in accordance with a set of clarifications provided. (Also see "*Afrigen MD: WTO IP Waiver Important From 'Freedom To Operate' Standpoint*" - Scrip, 23 Jun, 2022.)

Australia's Pharmaceutical Benefits Advisory Committee recommended the changes in response to the latest evidence on the "effectiveness and safety of the medicines, current usage data and the changing epidemiology of COVID-19", as per a statement from the government. More than 73,000 Australians have already benefited from these medicines, it added at the time.

Markets like India, however, appear to have seen a generally slow uptick in the use of molnupiravir going by IQVIA moving annual total data for March 2022. Favipiravir and remdesivir are the dominant antivirals the data suggest. (Also see "*Wave Of Molnupiravir Generics In India Amid Early Physician Cheer*" - Scrip, 29 Dec, 2021.) (Also see "*Will Pfizer's Paxlovid Go The Lagevrio Way In India?*" - Scrip, 23 Mar, 2022.)

Compelling Data

MSD's Peacock further drew attention to the fact that the initial molnupiravir trials were broadly done on non-vaccinated populations, with an eye on determining its "best utility".

Things are very different now for these products, with large parts of the world vaccinated. There

is a shift away from the utility of these treatments in terms of hospitalization and death, which have fallen although still far too high, more to other factors such as duration of infection, the executive said.

“There, we have some incredibly compelling data where we've been able to actually demonstrate that Lagevrio can after [a course of] five days , limit the positive infection at three, five and 10 days. That's an enormous impact, when we actually think about the economic consequences of COVID in a post vaccinated world,” Peacock maintained.

Earlier this year, Merck/Ridgeback presented additional exploratory patient subgroup and virology data from the MOVe-OUT study at the European Congress of Clinical Microbiology and Infectious Diseases. It included an analysis which showed that among patients with infectious virus at baseline, no patients who received Lagevrio had infectious virus at days 3, 5 or 10.

The Phase III MOVe-OUT trial studied Lagevrio versus placebo for the treatment of COVID-19 in non-hospitalized adults with mild to moderate COVID-19 who were at high risk for progressing to severe disease.

Peacock stressed that there's a “lot more to be understood” about how these antivirals work in the real world setting “once we get past the headlines” but clarified that isn’t to say that Paxlovid is not a “tremendous” medicine.

“It [Paxlovid] is. It has a unique mechanism of action and the world needs more than one medicine. But we are very confident in the clinical profile of molnupiravir,” he asserted.

On 30 June, Pfizer announced the submission of its New Drug Application to the US Food and Drug Administration (FDA) for approval of Paxlovid for patients who are at high risk for progression to severe illness from COVID-19, indicating at the time, among other data, that more than 1.7 million patients globally had been prescribed the oral treatment. The US firm had shipped more than 12 million treatment courses of Paxlovid to nearly 40 countries as of the end of May 2022.

Data from the US Department of Health and Human Services indicates that 2,380,646 courses of Paxlovid (including renal Paxlovid) and 407,484 courses of Lagevrio were administered during the period 17 December, 2021 – 10 July, 2022. The data, which is based on 83% of sites reporting as of 10 July 2022, covers all open distribution channels.

Efficacy Profile, Other Opportunities

MSD remains confident that molnupiravir’s mechanism of action will work against variants that are yet to come. While that obviously needs to be proven, but so far, the company hasn’t seen any change in the efficacy profile with different variants.

"That's an important thing, because we still don't know what the future shape of this disease will be. So having Lagevrio in the armamentarium is of critical importance to clinicians in the world."

With new COVID waves building up again, especially in Europe, the US and parts of Asia, the pandemic appears far from over and utilization of the antiviral is expected to rise alongside the new surges. (Also see "*Merck & Co.'s Solid Growth Turbo-Charged By Lagevrio For COVID-19*" - Scrip, 28 Apr, 2022.)

Merck Sees Options For Molnupiravir Past Pandemic

By Jessica Merrill

03 Feb 2022

The antiviral for COVID-19 added $952m to Merck's top line in 2021 and is forecast to deliver $5bn-$6bn in 2022, but CEO Davis sees potential for the product beyond the current pandemic, including potential combinations.

Read the full article here

"It's an incredibly difficult situation relative to other types of diseases where you get a relatively stable signal about what to produce and where to send it. Once again, more arguments as to why you want to have a multitude of suppliers in situations like this," the MSD executive added.

Lagevrio is also being studied for post-exposure prophylaxis in the global MOVe-AHEAD Phase III study evaluating the efficacy and safety of molnupiravir in preventing the spread of COVID-19 within households. The multicenter, randomized, double-blind, placebo-controlled trial also includes representation from some LMIC nations.

Earlier this year, Caroline Litchfield, Merck's executive vice president and CFO, also indicated that Lagevrio has shown its effectiveness against several variants of COVID-19, and could have applicability in many different coronaviruses.

"It has applicability in other respiratory-related viruses, such as RSV and influenza. On top of that, it's a product that has a great resistance profile, and it also does not have drug-to-drug interactions. So we are working really hard to ensure that Lagevrio plays an important role in preventing deaths through COVID-19," Litchfield said at the Bank of America Healthcare Conference.