INNOVATION COUNCIL

Innovation Council Q&A

The Development, Manufacturing, and Global Diffusion of MSD's COVID treatment, Molnupiravir

Julia Spencer, MSD

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nnovation Council's Jennifer Brant sat down with Julia Spencer of MSD to learn more about the development, manufacturing, and broad global diffusion of MSD's COVID treatment, molnupiravir.

Q Please introduce yourself and the company you represent, MSD.

A My name is Julia Spencer, and I am the Associate Vice President for Global Multilateral Engagement & Strategic Alliances at MSD. I am a public health expert with more two decades of experience designing and implementing public health programs, including 10 years working to strengthen the US government's public health emergency preparedness and response capabilities. MSD is a global healthcare company, based in the United States, that has been developing important medicines and vaccines to save and improve lives around the world for more than 130 years.

Q Can you tell us about your participation in the TRIPS Council Special Session in September 2023? It's what sparked my interest in developing this Q&A with you.

A Certainly. I was invited by the Chair to share MSD's experience as a co-developer and manufacturer of molnupiravir; this is an investigational oral COVID-19 antiviral marketed by MSD under the brand name LAGEVRIO. We refer to our branded product as "MSD produced molnupiravir".

We appreciated the Chair taking the initiative to solicit stakeholders' views and to include industry directly to inform discussions regarding the extension of the June 2022 waiver decision. Although COVID-19 is no longer a Public Health Emergency of International Concern, MSD continues to work with governments to support molnupiravir access to help address the ongoing challenges of COVID-19. During the session, I shared information about our company's global access strategy for molnupiravir.

Q Take us back to the start of the COVID pandemic. What was happening at MSD in 2020 as the pandemic was unfolding?

A In 2020, MSD moved quickly to mobilize our scientific expertise and resources to contribute to the global COVID-19 response. This included examining our current assets and establishing R&D partnerships for vaccine and treatment candidates – in total, we pursued 4 separate programs. Because we would need to produce any successful products at mass scale rapidly, we made substantial investments in securing supplies and our manufacturing capacity for all four candidates early and in parallel. This work was begun before we knew whether these candidates would be authorized for use and, in line with the high-risk nature of pharmaceutical development, only one, molnupiravir, advanced through early clinical development.

Q Out of multiple candidates, the only COVID product that MSD ultimately brought to society was molnupiravir?

A Correct.

Q Collaboration has been well-documented as essential to the unprecedente pandemic response. How did MSD work with others to develop and distribute molnupiravir?

A Partnerships characterized the molnupiravir story from the beginning. Molnupiravir is the result of IP created before the COVID-19 pandemic, then swiftly brought to market through IP-grounded partnerships with Emory University, Ridgeback Biotherapeutics, and others.

In November 2021 molnupiravir became the first oral antiviral in the world authorized for the treatment of certain patients with COVID-19. Rapid and equitable global access to molnupiravir was a key priority of MSD's from the start. We used a three-prong strategy, which we began to execute in early 2020, in parallel to our development program, to achieve this goal. This strategy included our own at-risk manufacturing scale up, generic licenses and manufacturing partnerships, and agreements with global procurement agencies. All of these actions were taken prior to or shortly after first regulatory authorization.

Q My understanding is that MSD started producing molnupiravir, in-house and with manufacturing partners, prior to securing regulatory approval. Is this correct? I assume this was a way to compress the time to market.

A Yes, that is correct. This was an important aspect of making molnupiravir available as quickly as possible, in light of the urgent circumstances.

By starting during clinical development, MSD's manufacturing network across three continents was able to make approximately 10 million molnupiravir courses available globally at the time of U.S. FDA emergency use authorization in December 2021. In parallel, we engaged proactively to secure supply agreements with approximately 40 governments in high, upper- and lower-income countries, utilizing a tiered pricing approach consistent with countries' ability to finance their health response to the pandemic. To date, over 5 million patients have been treated with MSD-produced molnupiravir.

Q What role did public funding play in getting molnupiravir to markets?

A MSD received no government funding for the development and manufacture of molnupiravir. Our investment in the drug's development and scale-up of manufacturing and supply was completely at risk. The public and non-profit sectors do provide important financial contributions to R&D, however, generally the private sector contributes the majority of R&D spending globally.

Q You mentioned MSD's global manufacturing network. Can you tell me more about how the network was established and how it operated?

A MSD made voluntary licensing agreements with eight Indian generic manufacturers more than six months before regulatory authorization to enable generic availability in 106 low- and middle-income countries, of which one quarter were upper-middle income countries. We worked closely with licensees to facilitate development and authorization of their products and supported bioequivalence studies for WHO PQ. We also engaged with funding partners to facilitate generic manufacturing scale-up: in October 2021, the Bill & Melinda Gates Foundation provided a volume guarantee of up to $120 million to several licensees to manufacture "at risk" so that significant generic supply was available at authorization.

To diversify the geography of licensed generic manufacturers, MSD entered into an agreement with the Medicines Patent Pool (MPP) in October 2021. MPP has issued sublicenses to 27 generic manufacturers in 10 countries across Asia, Africa, Europe, and North America, to supply molnupiravir to 106 LMICs. Both MSD's and MPP's licensing agreements allow licensees to supply to any country in the licensed territory with each licensee establishing its own individual price. More than 5.5 million treatment courses of generic molnupiravir

have been shipped by our licensees to 22 countries.

MSD also established local manufacturing and supply partnerships with companies in Brazil and China. Our partnership with Sinopharm in China is notable as it ensured that we could make supply rapidly available last winter during a period of spiking COVID-19 caseloads.

Q Can you describe the geographic coverage achieved by MSD's voluntary licensing?

A Licensing agreements, either bilateral or via the MPP, are designed to support and facilitate access in resource limited settings. Voluntary licensing and MPP agreements typically cover low- and lower-middle income countries. Our agreements not only cover these countries but also a large number of upper-middle income countries. Together – through bilateral voluntary licenses (VL), MPP sublicenses, and local manufacturing partnerships – our partners covered approximately 90 per cent of the population in LMICs.

Q In addition to voluntary licensing and geographically distributed manufacturing, did MSD use other strategies to ensure molnupiravir is available in all regions?

A Yes. MSD reserved approximately 30 percent (3 million courses) of our initial supply of MSD-produced molnupiravir for distribution to LMICs as a bridge to the availability of WHO pre-qualified generics for global health procurement organizations, which we made available through an agreement with UNICEF, announced just after US FDA authorization in 2022. This agreement was at our best access price for distribution to 107 LMICs. In May 2022, we committed to make available to USAID up to 2 million additional courses, also at our best access price.

Q Can you comment on the critique that molnupiravir was shipped to developed countries at the expense of patients in the developing world?

A The reality is quite different. Between supply reserved by MSD for global procurement bodies and courses shipped by our generic licensees, more courses of molnupiravir were available to LMICs during the first quarter of 2022 than were supplied to high-income countries in that timeframe. Because this question about whether there was impact of the VLs on LIC access was a topic of discussion during the TRIPS Council Thematic Session – I want to reiterate this point – that there were more courses of molnupiravir available to LMICs during the first quarter after first authorization than were shipped to HICs during this time period.

Q What challenges has MSD, or its partners, faced while working to produce and distribute molnupiravir where needed?

A Despite MSD's efforts to ensure equitable access to molnupiravir, slow procurement, lack of demand by global health organizations and governments, and the lack of widespread test-and-treat programs – barriers unrelated to availability or price – impeded access.

Q Tell me more about demand. Many health technology manufacturers emphasize the need for accurate demand forecasting. What happened with molnupiravir in this regard?

A ACT-A organizations — including the Global Fund, have been able to access MSD produced molnupiravir at the best access price under the UNICEF agreement, but demand signals and purchase requests have been significantly lower than expected. Global Fund recipient countries included in the UNICEF agreement could use Global Fund funding to essentially access this supply at no cost to the countries or their patients. Despite access to 3 million courses of molnupiravir in

January 2022, UNICEF only shipped the first molnupiravir supply in August 2022, and has deployed only 60,478 courses to 10 countries as of September 2023. However, earlier this year the Global Fund reallocated over $500 million of its remaining COVID-19 funds to other programs, citing a reprioritization by recipient governments. Despite this, we continue to engage with global procurers regarding expanding the geography covered under our agreements.

Though ample supply of molnupiravir was available, we noted significant geographical variability in how countries prioritized the scale-up of access to treatments.

Q What type of variability in demand did MSD experience?

A Well, in Asia Pacific, markets across income levels – including Japan, Australia, South Korea, Hong Kong, and Chinese Taipei – prioritized scale-up for COVID-19 antiviral treatment and entered into advanced supply agreements for MSD-produced molnupiravir, as did UMICs such as Thailand and Malaysia. LMICs, including Cambodia, Indonesia, the Philippines, and Vietnam, also moved rapidly to purchase supply of generic molnupiravir. We also further expanded our voluntary license territory to include Thailand to support substantial availability of generic courses in country through the government's COVID response.

In contrast, with some exceptions, MSD did not see significant demand in LMICs outside of Asia Pacific. For example, in MICs such as India and South Africa, no COVID-19 antivirals were recommended in government pandemic guidelines, despite antiviral recommendations from the WHO. In Latin America, with notable exceptions such as El Salvador, LMICs or UMICs in the region, including Brazil, Colombia, Costa Rica, and Ecuador generally did not prioritize scale-up of COVID-19 antivirals, despite availability of supply through MSD or its generic licensees. Specific examples illustrate this variability in demand.

Q Are you able to provide a specific example of challenges in a specific country that affected availability of molnupiravir?

A Yes, one specific example, Brazil, illustrates that achieving patient access requires multiple decisions in countries.

In Brazil, MSD's efforts did not advance due to decisions by Brazilian governmental authorities. MSD entered into a local partnership with the Oswaldo Cruz Foundation, for the local production, distribution, and sale of molnupiravir in Brazil as soon as emergency use authorization was granted. However, Brazil's health technology assessment agency did not recommend inclusion of molnupiravir in the public sector. As a result, for reasons unrelated to patent rights or price, MSD was not authorized to supply molnupiravir through the Brazilian public sector. We experienced similar challenges in other countries.

Q COVID is viewed today as less urgent a health crisis. What impact has this had on MSD and its partners?

A Eight of the 27 MPP licensees have terminated their licenses. I cannot speak to other companies' business decisions, however, according to recent analysis by the Center for Global Development, having too many manufacturers for a level of demand can limit returns and financial viability of generic producers. This is particularly true for more uncertain markets, such as those for COVID-19 oral antivirals and it is likely that these licensees are responding to market signals and turning their attention towards other therapeutic areas with more robust demand as was mentioned by other speakers during the TRIPS Council Thematic Session.

Q What other issues may have affected demand for molnupiravir?

A Lack of test-and-treat programs was one factor that impacted procurement and distribution of COVID-19 therapeutics. These programs are crucial in identifying eligible individuals for oral antiviral treatment within five days of symptom onset, encourages testing and simplify access to antiviral treatment, and can increase awareness among healthcare providers and patients. The challenges faced by LMICs in implementing these programs were discussed during a January 2023 White House Workshop. Cote d'Ivoire and El Salvador, included in MSD's license territory, successfully implemented test-and-treat programs using generic molnupiravir. However, scaling up and maintaining these programs in diverse settings proved challenging, demonstrating access and utilization difficulties for antivirals regardless of supply and affordability.

Q The TRIPS Council Special Session, where you spoke last year, focused on the possible extension of the June 2022 TRIPS decision on vaccines to cover also COVID therapeutics and diagnostics. Can you speak to the role of IP in MSD's pandemic response?

A Without the strong IP protections that allowed innovation and collaboration, MSD likely would not have molnupiravir available as a COVID-19 treatment today. The evidence shows sufficient supply for molnupiravir and sufficient procurement funds for ACT-A partners, so extending the TRIPS waiver would not improve global access to this treatment. However, it would undermine incentives for research-based companies to continue investing in future breakthrough and incremental innovations and could have ripple effects across all sectors that invest in research and innovation – including in future pandemic preparedness and response.

COVID-19 therapeutics can have multiple uses and indications and a waiver could be broadly interpreted, putting at risk investments to evaluate the potential of current COVID-19 therapeutics as well as medicines against other viral threats. For example, MSD has been evaluating molnupiravir against RSV, influenza, and other pathogens with pandemic potential and a waiver would be a strong disincentive to continue these efforts.

Q Thank you for your time – this Q&A session touches on many health policy issues. Any closing thoughts?

A Thank you for the opportunity to share our experience. I'd like to leave you with this: MSD supports faster and broader access to COVID-19 therapeutics, which is reflected in our access strategy. Our direct VLs in particular facilitated more rapid global access because we worked with the licensees and regulators to speed up their entry to market. As I indicated in my TRIPS Council presentation, a waiver of IP rights will not speed the production or delivery of treatments. Instead, we recommend that the global health community focus on addressing the many documented implementation and health system capacity challenges that have delayed access to COVID-19 therapeutics.