India COVID-19 Update: Antivirals, Eyes On HCQ-Azithromycin Data
Cipla Among Firms Prepping Favipiravir, Remdesivir, Baloxavir Generics
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Development work for antivirals such as Favipiravir and Remdesivir seen as potential treatments for coronavirus is underway in India, with the former's off-patent status making it more attractive. All eyes are also on data from a French study which highlights the potential of hydroxychloroquine and azithromycin as a COVID-19 treatment.

INDIAN FIRMS UP ACTIVITY AROUND POTENTIAL CORONAVIRUS TREATMENTS
As the world scrambles to repurpose approved treatments and develop new ones to tackle the deadly coronavirus, Indian firms are moving quietly alongside in sync, hoping to accelerate development activities or scale up plans for such potential therapies. Domestic firms are also keeping close watch on developments around an encouraging French study on the potential of hydroxychloroquine and azithromycin as a treatment for COVID-19.

Cipla Ltd., which has already indicated its readiness to move in quickly with generic supplies of AbbVie Inc.'s HIV combination drug Kaletra/Aluvia (lopinavir and ritonavir), has now tapped its long-standing ally, the Indian Institute of Chemical Technology (IICT), one of country's oldest national laboratories under the Council of Scientific and Industrial Research (CSIR), to develop Favipiravir, Remdesivir and Baloxavir. The antivirals are currently being evaluated as potential treatment options against the SARS-CoV-2 coronavirus.
"The first two are in advanced stages of finalization; Cipla is working very closely with IICT on this," **Cipla chair, Yusuf Hamied**, told *Scrip*.

CSIR-IICT has been developing the process for the active pharmaceutical ingredient (API) for the antivirals, while Cipla will then go on to make the API on a large scale and develop and commercialize the drugs, Hamied said. The indications are that a generic version of Fujifilm Toyama Chemical Co. Ltd.'s RNA polymerase inhibitor Favipiravir, which is off patent, could likely be the first of the antivirals off the block under the collaboration if all goes well. "It's a government-backed project and can be fast tracked in terms of the regulatory pathway," Cipla's chair maintained. Favipiravir (sold as Avigan) was first approved in Japan for pandemic influenza in 2014, and a licensed version is also being investigated in China, where COVID-19 was first detected in December 2019 in Wuhan. Favipiravir has been filed for investigation by China's Zhejiang Hisun Pharmaceutical Co. Ltd. as a generic drug, following the local patent expiry of the originator product. CSIR-IICT officials have been quoted in the Indian media as saying that Favipiravir and Remdesivir have already undergone some clinical studies and will not require much time to make since the "raw materials are readily available". Efforts around Baloxavir are being initiated now, they added.

Long-Standing Collaborative Links
Cipla and IICT (previously Regional Research Laboratory) share a long and successful history together; for instance a major IICT project that was considered a turning point for Cipla was the first manufacture and introduction in India of the fluoroquinolone antibiotics norfloxacin in 1987 and subsequently ciprofloxacin. Cipla also undertook, among other drugs, the manufacture in 1990 of omeprazole developed by IICT.
It is not, however, immediately clear how the Cipla-CSIR-IICT combine expect to approach the patent wall on Gilead Sciences Inc.'s investigational antiviral Remdesivir for the treatment of COVID-19; some experts reckoned that the product, which needs to be administered intravenously, would potentially be "more useful" for hospital and emergency cases. Last month, the US National Institutes of Health (NIH) commenced a randomized controlled trial for the treatment of COVID-19 patients with remdesivir; clinical trials of remdesivir are also ongoing in China. (Also see "COVID-19 Study Of Gilead's Remdesivir Using Ebola-Style Adaptive Platform Trial" - Pink Sheet, 17 Mar, 2020.)

Separately, Indian API company Lasa Supergenerics Ltd has also announced commencement of development of favipiravir in collaboration with the Institute of Chemical Technology (formerly the University Department of Chemical Technology) Mumbai, though things appear to be at an early stage.

Use Of Hydroxychloroquine, Azithromycin
Indian firms are also keeping close tabs on potential emerging opportunities from a French study which suggests that hydroxychloroquine treatment is significantly associated with viral load "reduction/disappearance" in COVID-19 patients and its effect is "reinforced" by azithromycin.

The study, published in the *International Journal of Antimicrobial Agents*, notes that despite some limitations including a "small sample size, limited long-term outcome follow-up, and dropout of six patients from the study," in the current context, the researchers believe that the results should be shared with the scientific community. Both hydroxychloroquine and azithromycin are widely available in India, with over half a dozen brands each including those of Cipla, IPCA Laboratories Ltd. and Alembic Pharmaceuticals Ltd.

"The government is fully in the picture; we've put ourselves at their disposal for whatever drugs they require," **Cipla's Hamied** said.

The Indian firm Alembic, on an investor call to discuss the impact of COVID-19 on the company, referred to the French study and said it was in a "wait and watch situation" and is constantly "scouring all medical updates" on any of its key products that can potentially play an active role in the treatment of COVID-19. "We are watching the scene to see if any more data comes out on azithromycin as we have a large interest and stake in that product," Shaunak Amin, managing director, said on the 20 March call.

In January this year, Alembic received final approval from the US Food and Drug Administration for its abbreviated new drug applications for azithromycin tablets 250mg and 500mg, a generic version of Pfizer Inc.'s Zithromax. Meanwhile, Dr Anil Pareek, president, medical affairs and clinical research at IPCA, noted that the French data represented the first clinical study showing effectiveness of HCQ alone and of a combination of HCQ and azithromycin. "These are encouraging results but small numbers; these results need to be confirmed by other investigators in a larger number of patients," Pareek told *Scrip*. (Also see "IPCA gets first approval for HCQ in diabetes" - Scrip, 2 Jan, 2015.) Interestingly, IPCA on 21 March informed Indian bourses that the US FDA had "made exception" to the import alert for the firm's hydroxychloroquine sulphate and chloroquine phosphate APIs manufactured at the unit in Ratlam and for hydroxychloroquine sulphate tablets made at the units in Pithampur and Piparia. The agency, however, said that the exception would be re-considered if the shortage implications change.

Spotlight On Chloroquine
Internationally, chloroquine, the antimalarial discovered by Bayer AG, has been in the spotlight as a key potential candidate for tackling some symptoms of COVID-19, though a gaffe by US President Donald Trump led to confusion around its approval as a coronavirus treatment; the FDA clarified that it hadn't been approved and that the agency had been working closely with other government agencies and academic centers that are investigating the use of chloroquine to reduce the duration of symptoms, as well as viral shedding that can prevent the spread of disease. Bayer is donating 3 million tablets of its Resochin (chloroquine) to the US for use in trials, while among other generic firms Teva Pharmaceutical Industries Ltd. is making donations of hydroxychloroquine sulfate tablets through wholesalers to hospitals in that market to meet the "urgent demand" for the medicine as an investigational target to treat COVID-19. Novartis AG is also making donations of generic hydroxychloroquine to support the global pandemic response.