

"Our drug is now an important treatment for HIV patients in China"

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High-potency active pharmaceutical ingredients (HPAPIs) like small molecules have been the longtime essentials for drug development. Small molecules constitute 90 per cent of drug sales being the primary active substance choice for pharmaceuticals. Frontier Biotechnologies is one such China-based global firm specialising in the accelerated R&D, development, and manufacture of complex small molecules for pharmaceuticals and biotechnology. Dr Changjin Wang, CEO and board member of China-based Frontier Biotechnologies, spoke with BioSpectrum Asia about emerging research and market prospects at small molecules for infectious diseases like anti-COVID and anti-HIV. Edited excerpts;

- **How do you describe Frontier's relentless efforts in antiviral therapeutics? How have the market trends and prospects been in this arena?**

For the past 20 years or so, we have seen many viral outbreaks across the globe. From SARS and MERS to the recent COVID-19, there aren't that many antiviral drugs available to help patients overcome these diseases.

Based on our experience and expertise in developing our HIV treatment, we decided to expand into developing a treatment for COVID-19 as well as other infectious diseases, though many are still in the early stages of development.

We believe that there is a huge unmet need in this area due to the difficulty in developing appropriate drugs for each type of disease. We are always open to learning and educating ourselves about new clinical challenges and seek to use our scientific expertise to address unmet needs in medicine via the expansion of our therapeutic portfolio.

- **What is your outlook for the infectious disease diagnosis and treatment market in China or the APAC region?**

We view infectious diseases as a major disease area and there is a growing need for more antiviral treatments, not only in this region but globally as well.

There are still tremendous opportunities in the diagnosis and treatment of infectious diseases and we are constantly trying to enhance our understanding of these new diseases in hope of developing new treatments that would benefit patients.

- **What is your approach to small molecule innovation and application?**

Based on our collective expertise and experience in developing antiviral protease inhibitors, we decided to develop an antiviral drug for COVID-19 – FB2001 (bofutrelvir), as we believe that it is a more effective treatment option versus antibody therapy, especially against the different COVID-19 variants.

In September we announced positive results from the Phase 1 clinical trial of our drug candidate, FB2001 – a small molecule inhibitor of coronavirus main protease (Mpro) – in healthy adult volunteers. Clinical studies have shown FB2001 to be safe and well tolerated among trial participants.

FB2001 has demonstrated in vivo antiviral activity in the lung and brain tissue of the SARS-CoV-2 mouse model without the need for pharmacokinetic boosting. Therefore, it holds great promise as a treatment for acute COVID-19 as well as long-COVID, both of which will be evaluated in further follow-up studies.

Frontier Biotechnologies is also developing a pulmonary formulation of FB2001 that could be used in outpatient settings for the treatment of mild COVID-19, as well as for post-exposure prophylaxis. When inhaled directly into the respiratory tract and lungs, the tissue concentration of FB2001 is much higher than that in plasma; hence, the onset of action and viral clearance could potentially be faster than that of oral therapy.

Additionally, we hypothesise that a pulmonary formulation might be more effective in outpatient settings as an inhaled drug can reach the respiratory tract and lungs directly, resulting in a faster onset of action and viral clearance. This is currently in development, and we hope that our programme's success may help decrease the disease burden and improve patient outcomes in the long run.

For hospitalised patients who are receiving many drugs at the same time, we strived to develop a single-agent drug that can achieve effective treatment doses without the use of a 'booster' component to reduce the risk of drug-drug interactions. Bofutrelvir is currently in Phase II and III trials, involving around 1,200 hospitalised patients in clinical centers worldwide.

- **Could you shed some light on your efforts in developing the first long-acting anti-HIV fusion inhibitor and subsequent market penetration?**

Frontier Biotech started off with the idea of creating albuvirtide, which is our first product on the market. This was made possible with the help of Dr Dong Xie, one of our co-founders, who has extensive experience in HIV drug discovery development.

We believed that long-acting injectables would be key to helping patients as they could reduce pill burden and improve treatment adherence, at a time when most treatments were in the form of oral pills.

It took us a really long time to develop our HIV treatment, but we persevered, and our drug was approved for use in 2018 by China's National Medical Product Administration.

Once approved, we began our commercialisation efforts in China with a specialised team of about 100 people, who had to do a lot of market education with the healthcare community and patients owing to unfamiliarity with long-acting injectables at that point in time.

Our efforts paid off as our drug is now an important treatment for HIV patients in China. We are seeking marketing authorisation for Albuvirtide from health authorities in many countries and have already received approval from Ecuador, Cambodia, Malaysia, and Azerbaijan. We hope to expand commercialisation to many countries in Asia, Europe, South America, and Africa.

- **What is your stake in Asia for Active Pharmaceutical Ingredient (API) synthesis and preparation, especially in the development of new long-acting peptide drugs?**

We have recently built two large-scale manufacturing facilities in Nanjing and Chengdu. The Chengdu plant allows us to have one of the biggest peptide API manufacturing capabilities in China, with a production capacity of 250 - 1,000 kg of API peptide drugs annually. These facilities support not only the production of our own approved products but also future pipeline molecules. Other companies can also work with us to leverage our manufacturing capabilities.

- **What's your current innovative drug product pipeline for FY 22-23?**

We have a number of products that are currently in our drug development pipeline:

- In the HIV space, we have the FB1002 combination drug (Albuvirtide + 3BNC117) that is undergoing three Phase II trials in the United States and China.
- For COVID-19, we have FB2001 which is currently undergoing Phase II and III clinical trials globally.
- We also have FB3001, a novel topical patch for the management of pain and inflammation that is about to enter a Phase III trial.
- FB6001, a therapeutic peptide vaccine targeting PCSK9, is an anti-hypercholesterolemia / low-density lipoprotein agent, currently in preclinical development.

We are constantly leveraging our expertise to discover and develop new drugs that help ease patients' disease burden. We are aiming to grow our presence globally, with the hope of attracting new talents and taking our capabilities to the next level.

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