BioRegio STERN conducted an interview with Dr. Rainer Lichtenberger, co-founder and CEO of Atriva Therapeutics GmbH, which recently announced the approval of a phase II trial on COVID-19 patients. Led by the Charité university hospital in Berlin, the trial will test the efficacy, safety and pharmacokinetics of ATR-002 on 220 patients in Germany and around the world. This drug developed by the biopharmaceutical company founded in Tübingen is intended to treat patients who are moderately or seriously ill with COVID-19.

“The entire biotech sector is now showing what it’s made of!”

Atriva Therapeutics GmbH was working on an active ingredient to inhibit flu viruses. What made you decide to use this as a basis for developing a COVID-19 drug?

Based on our knowledge of flu viruses, it made perfect sense to ascertain whether our general approach could also produce successful results with COVID-19. ATR-002 has a special and unique mode of action. It attacks the structures in the host cell that are important for the replication of this entire family of viruses – referred to as RNA viruses – including both the flu virus and the SARS viruses that cause COVID-19. On the one hand, our drug has a proven antiviral effect, making it impossible for the virus to replicate due to the absence of the necessary cellular apparatus. On the other – and this is its unique feature – it influences the immune system in such a way as to prevent the dreaded excessive immune response that leads to a significantly increased release of cytokines and can be even more fatal for COVID patients than for those suffering from flu.

When did you learn about the new virus and when did you start developing a drug to treat COVID-19?

The world's number one market for antivirals besides the USA is China. The close scientific contacts we'd established with Chinese partners and companies because of our flu drug meant we were already aware in January of the severity of the outbreaks in Wuhan. We then began testing at our labs in February and, eight weeks later, we were certain that ATR-002 is also effective against SARS-CoV-2. We started preparing for the clinical trial back in mid-March and got in touch with Professor Martin Witzenrath from Charité, Europe's largest hospital specialising in pulmonology and infectious diseases.

Did you receive any special support to speed up the development of a COVID-19 drug?

Government funding naturally focused on vaccine research to start with. Perceptions are now changing, though, and support is being extended to treatments with the aim of reducing the extremely high mortality rates being seen at hospitals. These were totally unexpected and exceeded our worst fears. Two months ago, hardly anyone would have thought it possible that we would have up to 1,000 daily deaths. Nobody predicted how the pandemic would take hold. The risk of making mistakes is huge. Germany has continued to fare better than many others, but we mustn't throw that away now. A three-step approach is required. First of all, we must minimise contact and optimise personal protection. The second and most important step is the vaccine. And thirdly, we need treatments to minimise the number of serious cases so that our healthcare system continues to cope. The Ministry of Health has now realised this. Amongst other things, we're obtaining a loan from the European Investment Bank (EIB) that will provide Atriva with up to 24 million euros for the development of our drug to combat COVID-19.

When will it be possible to treat regular patients with ATR-002?

Ever since we announced the start of the phase II trial, we've been receiving calls from patients and their families asking for treatment. Regrettably, we're still having to ask them to wait, but we're endeavouring to have the drug

available to patients by the end of this year. The initial patients selected for the trial at Charité are to be given ATR-002 in January, as soon as we have the stamp of approval. We're expecting to treat around 30 patients per week given that hospitals currently have more than enough to do without clinical trials. Despite this, Professor Witzenrath has allocated a doctor and a study nurse specifically for this purpose. We estimate that we'll have treated the requisite 220 patients by the end of the second quarter of 2021. We'll then need to keep them under observation for a period of 90 days, during which we'll see whether or not the drug is effective.

ATR-002 is now starting to be administered to sick people. A total of 1,000 patient years is normally required to establish a drug's safety, but that's more difficult to insist on in an emergency situation such as this. Nonetheless, the risk-benefit analysis must be totally convincing and all questions raised by the responsible authorities must be answered.

How important is it to develop highly effective antiviral treatments for the global pandemic?

According to experts, the southern hemisphere is at particular risk of experiencing a third wave once the colder months return there. And we'll be unable to vaccinate the entire population as quickly as we would like. If, for example, this more infectious virus mutation from the UK becomes widespread, having 60 per cent of the population vaccinated won't be sufficient. We'll need to achieve a level of 90 per cent – despite the current vaccine scepticism …

Other risks are also constantly emerging, including tropical diseases such as dengue fever and hantavirus. The warmer the climate becomes, the more Europe, too, will be affected by diseases of this kind, so we need to find highly effective antiviral treatments as quickly as possible.

Is it true to say that you and the entire biotech sector are currently under a great deal of stress and have an unprecedented workload?

Yes, there's lots of work to do, but I'm extremely motivated, just like all my colleagues. We're all being spurred on by the desire to play our part in fighting the coronavirus pandemic, and the entire biotech sector is showing what it's made of. Comparing biotechnology with the pharmaceutical industry is like comparing a speedboat with a supertanker and illustrates that hopes are currently being pinned on what our sector is coming up with. Biotech research and activities are finally gaining the recognition and appreciation they deserve – a real paradigm shift. The population is realising that salvation doesn't come in the shape of SUVs with petrol engines, but rather smart technologies that make the world a better place. That applies to both the healthcare sector and environmental protection. Germany has finally once again provided convincing proof of its global scientific prowess in terms of both vaccine development and treatment. Four of the six most important approaches come from companies either based in Germany or with German roots. What we still need to do is to grasp our opportunities and shape our further development in such a way as to create a life sciences industry that has a similar international standing. We've had a wake-up call and I hope we don't simply hit the snooze button.

How do you see the further development of Atriva Therapeutics GmbH?
We currently have two sites – one in Tübingen and one in Frankfurt/Main. The excellent links at the clinical site in Frankfurt are vital for international collaboration, but we're also envisaging further expansion of our lab facilities in Tübingen. The loan from the EIB has secured the necessary funding to complete this phase II trial in its entirety.

The active ingredient candidate ATR-002 is the Atriva product at the most advanced stage of development. Are you already in a position to announce further candidates in the pipeline?
The other active ingredient candidates we're working on primarily concern additional indications for the initial candidate, such as tropical viruses or hantavirus. We've now carried out tests on eight different viruses, including

various strains of bird flu, and we've established that our mode of action is on such a broad footing that it's effective in all these scenarios. That means we're also in the perfect position when it comes to pandemic awareness, making sure our healthcare system is prepared for new, unknown viruses. In the medium term, we're planning a wider active ingredient platform.

About Atriva Therapeutics GmbH
Atriva Therapeutics, founded in 2015, is a biopharmaceutical company pioneering the development of host-targeting antiviral therapies set up by a team of leading scientists in viral research and seasoned industry experts. The Company aims to develop a therapy platform to treat severe respiratory diseases induced by RNA viruses with a high unmet medical need, such as influenza and COVID-19. The Atriva lead product ATR-002 is a first-in-class host-targeting agent which inhibits viral replication in influenza and favorably modulates the body's immune response. ATR-002 is under clinical development and has successfully completed a Phase I trial to demonstrate safety and tolerability in healthy subjects. The Company has obtained regulatory approval for a Phase II study to evaluate efficacy in hospitalized COVID-19 patients; a Phase II study in influenza is planned to start later in 2021.
The Company owns eleven patent families with broad international coverage related to the use of MEK inhibitors and other kinase inhibitors for antiviral therapies. The patent life runs through 2041. Atriva Therapeutics is located in Tübingen and Frankfurt, Germany.

About BioRegio STERN Management GmbH
BioRegio STERN Management GmbH promotes economic development in the life sciences industry, helping to strengthen the region as a business location by supporting innovations and start-up companies in the public interest. It is the main point of contact for company founders and entrepreneurs in the Stuttgart and Neckar-Alb regions, including the cities of Tübingen and Reutlingen.
The STERN BioRegion is one of the largest and most successful bioregions in Germany. Its unique selling points include a mix of biotech and medtech companies that is outstanding in Germany and regional clusters in the fields of automation technology and mechanical engineering.

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