

Bulgarian biotech startup close to breakthrough in COVID-19 treatment efforts

As a vaccine is not available and the number of coronavirus patients worldwide is growing by the hour, Micar Innovation (Micar21.com) may hold the key to defeating the 2020 pandemic.

Recent weeks have seen the scientific community worldwide working around the clock to decipher the mechanisms behind the COVID-19 pandemic in a bid to find an efficient treatment and a vaccine. In this constantly changing situation of crisis, a team of Bulgarian scientists, part of biotech startup Micar Innovation (Micar21), made the headlines in the small CEE country and beyond, stating they may be closer than anyone else to discovering a cure.

"Micar21's team of scientists can design a suitable specific inhibitor molecule that could prevent ACE2 from connecting with COVID-19 S1 spike protein within 30-45 days," company founder Filip Fratev said in a statement. "This would be an overall solution to treat other similar viral infections, too", he added.

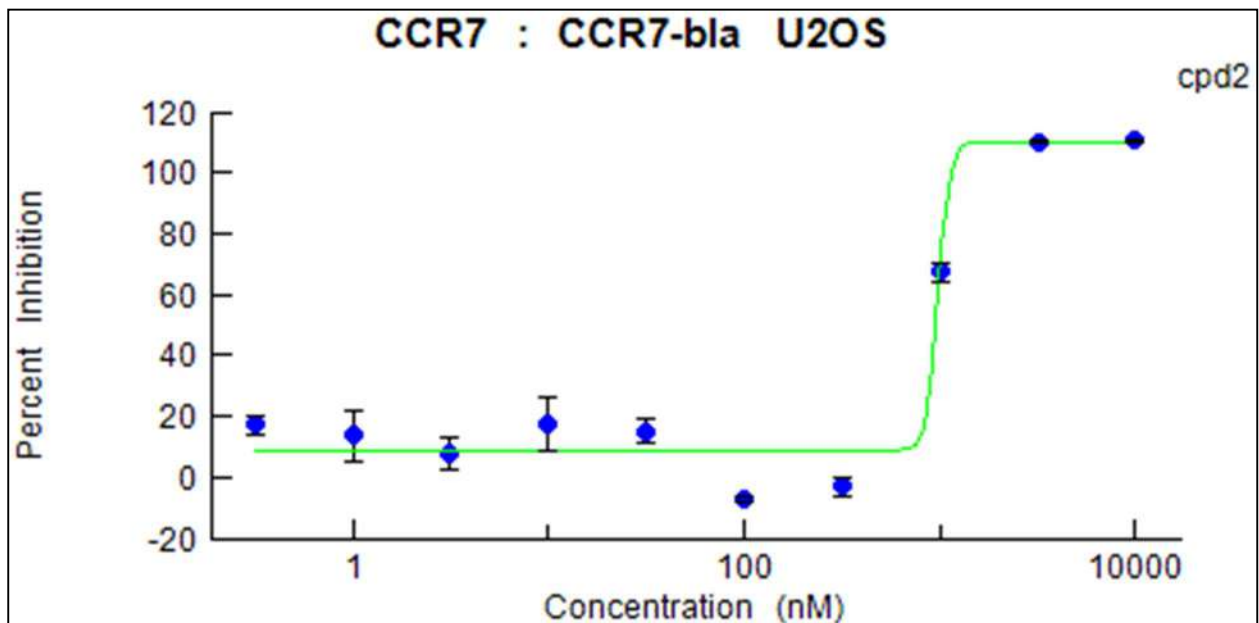
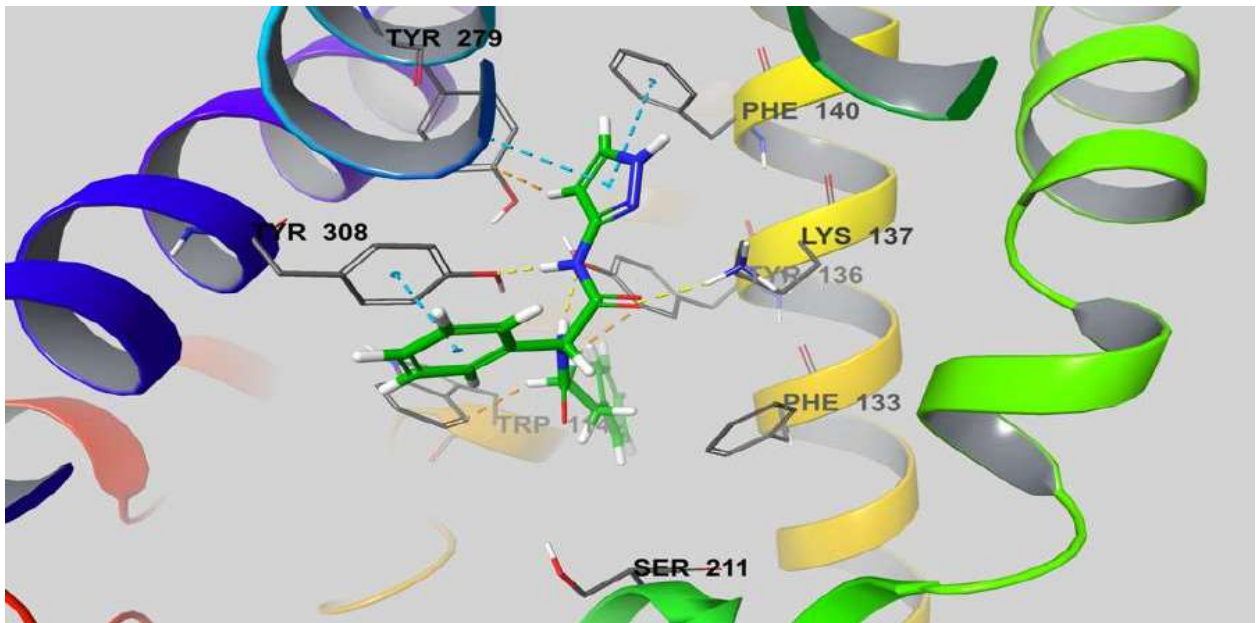
A month or so sounds like a strikingly short period of time to achieve such results, considering the long and complicated mechanisms usually involved in molecule design. On average, designing a new drug molecule takes about 18 months.

COVID-19, CCR receptors and Micar21's approach

From the very beginning, Micar21's team has been concentrated on the CCR1-CCR10 cellular receptors, which control the migration and positioning of immune cells in tissues and are critical for the function of the innate immune system.



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The (un)expected leadership factor

Micar21's unique advantage lies in their patented drug discovery platform that combines AI and scientific research to deliver streamlined, highly-optimized, and, most importantly today, fast results.

"The company was founded four years ago, and we spent the first two years fully optimizing our drug molecule design platform. We gradually began to improve each step along the way by using a specific innovation, an improvement that we always validate through scientific publications in reputable scientific journals with the highest impact," said Fratev.

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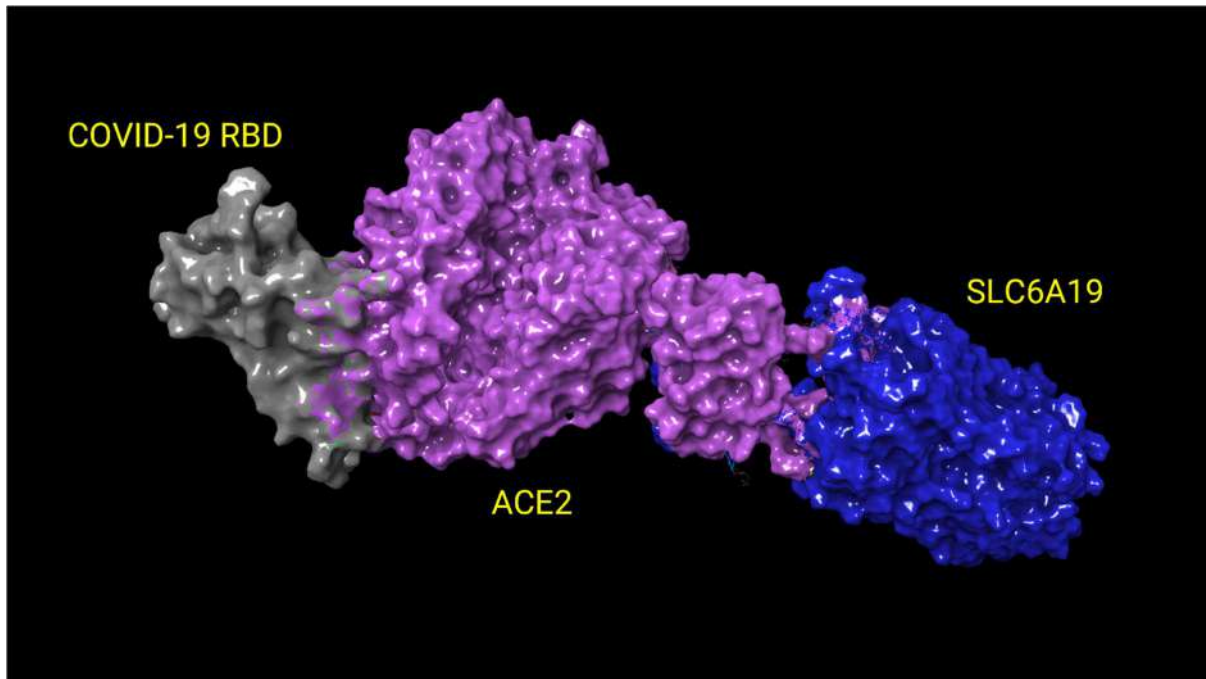
Another unexpected benefit (at least for the public) of the startup today is its market niche. Four years ago, when the company was launched, its business model was to focus on the so-called “orphan diseases” – rare conditions with a market share that is not large enough to attract support and resources for discovering treatments. They chose this segment as it was largely unattractive for players in the industry, looking for fast and big profits, and competition there was low, giving them a chance for a breakthrough.

Two of these receptors in particular, CCR5 and CCR7, have certain mutations that make individuals with these mutations resistant to diseases such as HIV. CCR5 has been at the core of Micar21’s research, and the company already has a breakthrough with a novel drug molecule for the treatment of chronic pain. The project belongs to Bolka Pharmaceuticals, a Micar Innovation spin-off that develops MIC4578 drugs.

Recent scientific reports evidence the resemblance in immune response between COVID-19 and HIV’s cell impact and penetration. Based on them, Micar21’s scientists decided to urgently refocus their efforts on researching the virus in a bid to utilize their experience and knowledge to help humankind in this difficult battle. Hard work is already underway to develop a set of new bioactive molecules to combat the disease. A lead compound, a CCR5 antagonist, has already been designed.

Efforts underway

Micar21 has already discovered and patented drug molecules which are good CCR5 and CCR7 antagonists and is working to optimize them to achieve better binding and selectivity to the target proteins. On the other hand, recent scientific research shows that COVID-19 enters the cell through another membrane protein – ACE2. There are many approved medicines that inhibit the ACE protein (most of them are used to treat cardio-vascular diseases and high blood pressure), but they are not selective in terms of ACE2 and cannot be used to treat viral infections. Moreover, the enzymatic ACE2 activity does not affect the S1 spike protein-ACE2 binding thus the virus entering into the human cell. A specific inhibitor needs to be developed to prevent COVID-19 and ACE2 interactions, which should bind to specific surface ACE2 pocket, without affecting other physical processes going on in the human body. Micar21’s scientists are confident they can achieve that within 30-45 days and optimize the molecule for clinical trials within several months.

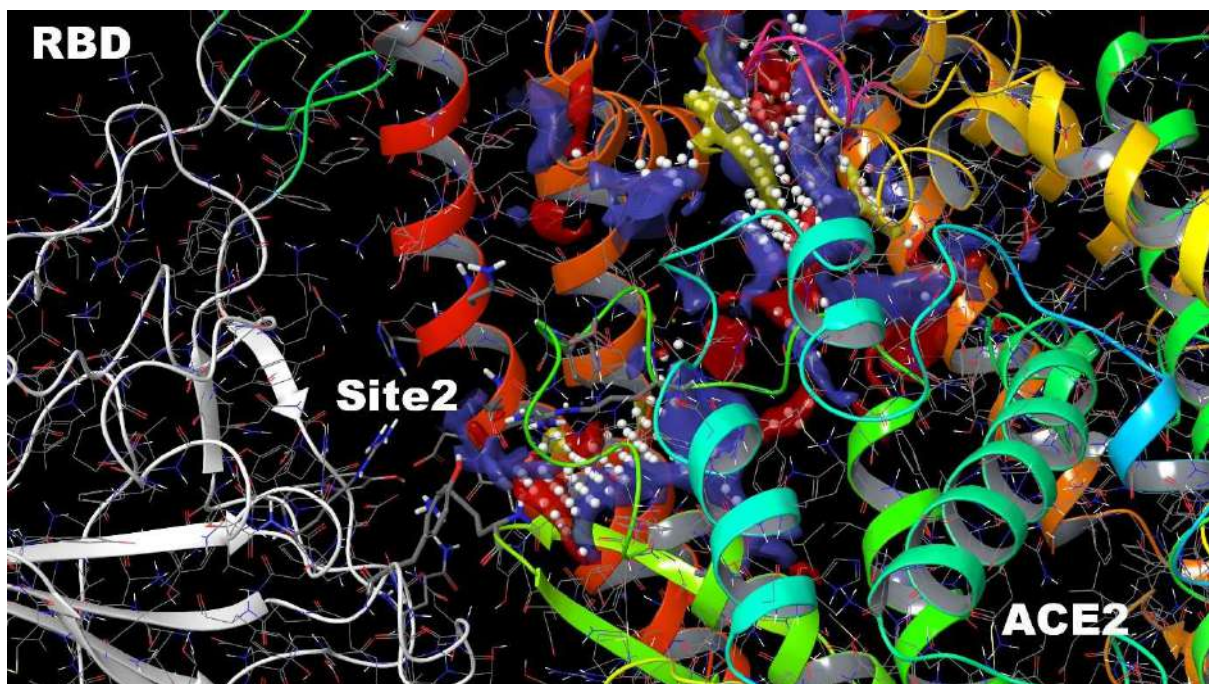
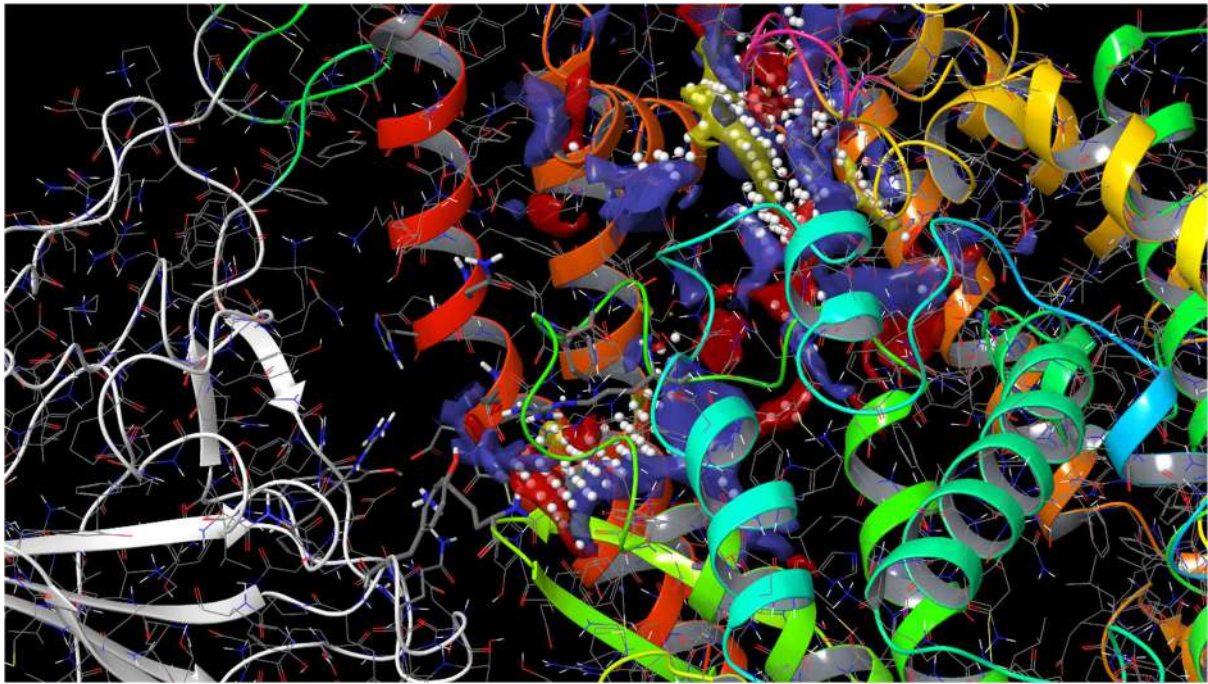


Another, even faster option is to use a molecule that has already been developed by Micar Innovation for modulation of the so called genes *SLC6A5* (GlyT2) and *SLC6A14*. A study on this topic has been published in *ACS Med. Chem. Lett.* journal last year. It also binds to the homologous natural transporter B⁰AT1 (*SLC6A19*) which is involved in the S1-ACE2 complex formation. In fact, recent cryo-EM structures showed the structure of *SLC6A19* which is attached to ACE2 along with S1 receptor binding domain of COVID-19. Thus, it can be a promising molecule for treating COVID-19. In this case, the company can generate a set of preclinical data in a matter of weeks and the compound can be also tested directly on the virus.





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Support, anyone?

Apart from working 24/7 on its scientific research and monitoring closely the global COVID-19 crisis, Micar21 is currently connecting with fellow-scientists, service providers, and institutions in Bulgaria and abroad in a bid to secure support for its ongoing efforts. Its breakthrough made a splash in local media but any attempt to secure funding from the government in the poorest EU country, particularly amid the expected harsh economic blow, have hit a dead end. But the team has no intention to give up.

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Due to the urgency of finding a therapy for Covid-19 Micar 21 seeks grant and equity funding to speed up the hit-to-lead development, lead identification, pre-clinical and clinical lead development. The company is searching for opportunities for partnership with established pharmaceutical companies and CROs with whom to enter into a licensing agreement and (co-) develop the treatment.

"We have drawn up an action plan. We are constantly communicating with colleagues from different countries. Perhaps this is the moment to thank the Bulgarian scientific community outside our country, which offers its assistance and with whom we are working together", said Fratev.

As with many other businesses in the small CEE country, Micar21's hopes lie with the EU's funding opportunities such as the EIC Accelerator and IMI2 - Call 21.

"We hope that the European institutions will be much more active and responsive than the Bulgarian ones," said Fratev.

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