There are seven known types of coronavirus (CoVs), which include 229E and NL63 (Genfa Alphacoronavirus), OC43, HKU1, MERS and SARS (Genus Betacoronavirus). While 229E, NL63, OC43 and HKU1 typically infect human population, SARS and MERS epidemics in 2002 and 2012 respectively were results from transition of the virus from animals to humans, raising significantly the mortality rates of the diseases. The recent 2019-nCoV (COVID-19) pathogen that has emerged in China has been characterized as a new member of the Betacoronavirus genus, closely associated with several types of coronavirus in bats, as well as a severe acute respiratory syndrome coronavirus (SARS-CoV). Compared to SARS-CoV, COVID-19 appears to be more easily transmitted from person to person, and has spread across multiple continents, leading to the WHO's Global Health Emergency Declaration on Novel Coronavirus, followed yesterday by a **pandemic status**, all of which reflecting the impact of the virus as an international problem. The evolution of 2019-nCoV remains elusive. Most closely, COVID-19 resembles the coronavirus strands that caused the epidemics in 2002 and 2012, which is 97.8% and is quite significant. However, there is still more than 17% difference, especially in the parts related to protein functions, which makes it a different virus altogether.

Currently, the global scientific community is working intensively to unravel the characteristics and features of the new virus, which will help them to identify a treatment and a vaccine. The complete crystal structure of COVID-19 has been obtained days ago by cryogenic electron microscopy and published in one of the world's most prestigious scientific journals *Science* on March 4th, 2020. This provides many new opportunities for scientists to create vaccines and medicine.

The company Micar Innovation (Micar21) has a strong track record in the development of drug molecules that bind to the so-called chemokine receptors[1], in particular CCR2, CCR5, CCR6, CCR7, and CCR9 receptors. Based on previous scientific reports on the similarity of action and entry through cellular walls that exists between COVID-19 and HIV viruses, Micar Innovation scientists have redirected their efforts from developing a potent CCR7 antagonist to one that has dual action, including inhibition of the CCR5 receptor. The latter is responsible for the entry of the HIV virus into the cell. Most HIV infections begin when the virus is pressed against the CD4 glycoprotein on the surface of CD4-positive T cells. However, in order for the infection to occur, the virus must also attach itself to a protein from the secondary cell wall. This second protein is CCR5. When HIV-1 is bound to both CD4 and CCR5, it fuses to the cell. **Micar Innovation has discovered and obtained a patent for a drug candidate that is a good CCR5 antagonist.** It is yet to be optimized, meaning to improve even further its binding and selectivity properties to target proteins, as well as its overall pharmacological characteristic.

On the other hand, following the publication of the scientific article mentioned above, as well as one in the journal *Cell Discovery*, dating from February 24th, 2020, it became clear that COVID-19 mainly uses another membrane protein for cellular entry, namely the angiotensin-converting enzyme 2 (ACE2). There are numerous approved drugs that inhibit homologous ACE protein. They are intended primarily to treat cardiovascular disease and high blood pressure and are not selective for ACE2, therefore cannot be used to treat viral infections. Moreover, couple of days ago, there was an urgent report stating that people taking ACE inhibitors should immediately cease reception, because inhibiting ACE leads to an increase in ACE2 protein levels 3 to 5-fold, thus increasing virus entry into cells, which leads to increased mortality rates among patients.

Therefore, based on the structure of the virus already obtained, a specific inhibitor should be developed that only interferes with/inhibits the interaction of COVID-19 and ACE2 and does not affect other physiological processes. **The scientific team of Micar Innovation is committed to finding a suitable and specific inhibitor to prevent ACE2 from binding to COVID-19 within 30-45 days,** which would be a

[1] Cytokine receptors found on the surface of certain cells that interact with a type of cytokine called a chemokine.

complete solution for other viral infections as well**.** The candidate molecule is scheduled to be optimized and submitted for clinical trials within a couple of months. It is possible to use as the basis for a new drug candidate the already existing (not yet approved for medicinal use) MLN-4760 molecule, which will be then modified and optimized using Micar Drug Discovery Platform up to the point to be used as a primary drug ingredient. **In this case, Micar21 can generate a set of drug molecules in just a matter of weeks,** which can subsequently be tested directly on the virus, as part of cellular tests, in a suitable laboratory in Bulgaria or abroad. The latter will probably require assistance from the relevant agencies or ministries.

Another key information from recent research is that ACE2 acts in cooperation with the B0AT1 protein, also known as SLC6A19. **Currently, Micar Innovation1 has a developed molecule that binds and inhibits the structural homolog of SLC6A14 as well as SLC6A5 (*ACS Med Chem Lett. 2019 May 22; 10 (6): 904-910*).** This molecule may also inhibit SLC6A19, if not it can easily be optimized for that purpose.

After the first cases of infection on the territory of the Republic of Bulgaria, the scientists from Micar Innovation initiated an accelerated program to identify and develop a treatment for COVID-19.

Based on the above information, the company's action plan is as follows:

1) Optimization up to phase of Clinical Tests of the already discovered Micar Innovation drug molecule antagonist of CCR5.
2) Optimization up phase of Clinical Tests of the already discovered Micar Innovation drug molecule inhibitor of SLC6A5 to that of SLC6A19.
3) Discovering of a suitable inhibitor of the interaction between COVID-19 and ACE2, or – even more efficiently - transforming an already existing molecule (MLN-4760) into a new drug that modifies this interaction.

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