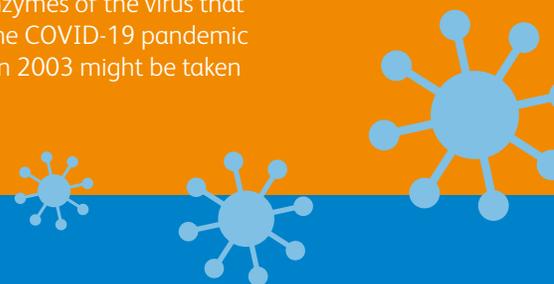


Pfizer COVID-19 Response: Protease Inhibitor

In 2003, Pfizer scientists identified and began the pre-clinical evaluation of an antiviral compound for potential use in addressing the Severe Acute Respiratory Syndrome (SARS) epidemic, which was caused by a coronavirus similar to the one driving COVID-19 pandemic today. The compound they identified was shown to be a potent inhibitor of a protease enzyme that coronaviruses need to replicate. Since the protease enzymes of the virus that causes the SARS epidemic and the COVID-19 pandemic are very similar, at the onset of the COVID-19 pandemic Pfizer scientists began to urgently work to determine if the antiviral compound identified in 2003 might be taken into the clinic to potentially treat COVID-19.

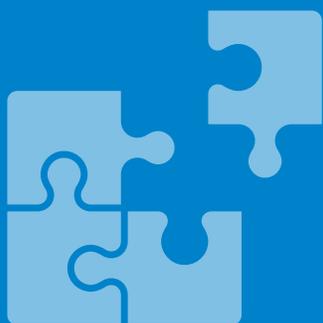


Targeting a critical, protein cutting enzyme

When a virus infects the body's cells, it takes over the cell's internal machinery in order to produce viral proteins to make more copies of itself. Initially, the infected cell forms a single viral protein chain, like a long string that is mostly non-functional. The protease enzyme clips the protein chain in specific areas to produce functional pieces that are critical for the virus to replicate and survive.

Protease inhibitors are a class of antiviral drugs that block this protein-cutting process, and thus stop a virus from multiplying. Protease inhibitors are a proven class of medicines that are widely used to treat HIV and the hepatitis C virus.

Pfizer recently confirmed in initial screening that a lead compound and analogues are potent inhibitors of the 3C-like (3CL) protease of SARS-CoV-2, the coronavirus that causes COVID-19. As described below, the protease inhibitor binds to the active binding site of this essential enzyme. Any mutation in this binding area, which could potentially render a drug ineffective, would also likely negatively impact the survival of the virus.



Finding the right fit

In 2003, scientists produced a 3-D crystallography structure of the SARS protease to guide their design of a compound that fits into the protein pocket binding site. Through an iterative process of designing, synthesizing and testing thousands of prototype compounds, they developed their current lead compound.

All-hands-on-deck effort

Even before confirming that their current lead has potential to treat COVID-19, Pfizer has made investments in the materials that will be needed to move forward into the clinic as quickly as possible should the pre-clinical work support beginning a clinical trial. In addition, academic researchers and other experts in the field are collaborating with Pfizer to help accelerate the process.

