

# New TMPRSS2 inhibitors as antivirals for coronavirus and influenza pandemics



## KEY ACHIEVEMENTS

- Developed potent and specific small molecule inhibitors for the human transmembrane serine protease TMPRSS2.
- Inhibitor family patent protected.

## KEY COMPETITIVE ADVANTAGES

- TMPRSS2 drives the predominant mode of viral entry during lung infection of corona and influenza viruses.
- Inhibiting TMPRSS2 is a more robust antiviral strategy than inhibiting viral targets, as the former is not subject to mutations.
- TMPRSS2 has no known indispensable functions and no toxicities are expected from its inhibition.

**TMPRSS2 inhibition is potentially safer than existing antivirals and more suitable for future pandemics.**

## ONGOING ACTIVITIES

- Hit-to-lead optimization.
- In vitro validation.

## INTELLECTUAL PROPERTY

PCT/EP2023/061344 SUBSTITUTED ARYL ESTERS OF COUMARIN-3-CARBOXYLIC ACID AND THEIR USE AS HOST CELL PROTEASES INHIBITORS

Corona (SARS and MERS) and Influenza (A and B) epidemics or pandemics have occurred worldwide throughout the early 21st century. Vaccination in combination with antivirals has been effective in controlling them. Nevertheless, new viral mutations could make vaccines and existing antivirals ineffective. This highlights the need for novel antivirals that target host mechanisms, which are less prone to mutation.

TMPRSS2 is a transmembrane serine protease highly expressed in the respiratory epithelia, where it drives the predominant mode of viral entry by membrane fusion at the cell surface during lung infection of SARS-CoV-2, MERS-CoV, influenza A, influenza B, and other coronaviruses. As a result, this protein is an attractive target for new antiviral agents, as inhibiting its proteolytic activity is expected to block viral entry. Most notably, inhibiting this host serine protease is a safer antiviral strategy than inhibiting viral proteases, as the former is not subject to mutations. TMPRSS2 inhibitors are being tested in clinical trials to assess their efficacy for SARS-CoV-2 infection. Nevertheless, these molecules lack selectivity and present poor bioavailability.

The team of Dr. Bernard Pirotte at the University of Liège has more than 30 years of experience in the design, synthesis, and hit-to-lead process of small molecules targeting human proteases. He has developed highly potent and specific small-molecule TMPRSS2 inhibitors. The molecular structure of these molecules bound to TMPRSS2 has been determined, which at present leads the development of improved variants.

## PARTNERSHIP SOUGHT

- Collaboration to select and validate hit preclinically and take it to the clinics.
- License agreement.

