

## BROAD-SPECTRUM THERAPEUTICS FOR VIRAL DISEASES: A MEDICAL COUNTERMEASURE PLATFORM FOR EMERGING THREATS

# A Broad-spectrum Antiviral And Immunomodulatory Agent Against Covid-19 And Disease-x

Sherine Abdelmawla Akanocure Pharmaceuticals, Inc.

Mohammad Noshi Akanocure Pharmaceuticals, Inc.

Akanocure is a drug development platform company working on novel structurally diverse and complex macrocycles against orphan and unmet needs in oncology, infectious diseases, and immunology. Akanocure, in collaboration with UTMB at Galveston, identified a small molecule macrocycle as a host-directed broad-spectrum antiviral and immunomodulatory agent. Inhibition of such host factor efficiently shuts down viral replication, in addition, it is proven to correct the toxic immune response induced by some viral infections (e.g., COVID-19 infections) by inhibiting production of pro-inflammatory cytokines, restraining Th17, and promoting Treg, thus stopping hyperinflammation, autoimmunity, and multi-organ damage. Akanocure's compound was not cytotoxic at the highest concentrations used in the experiments. It demonstrated the proposed broad-spectrum activity by efficiently shutting down the replication of COVID-19 (50% inhibition at 10 nM) and other notorious, deadly, and difficult-to-treat viruses like Sudan Ebola (150X more efficient compared to favipiravir) and Nipah viruses, all of which are on the WHO list of diseases and pathogens that are prioritized for R&D in public health emergency contexts. The WHO recognizes these viruses as posing the greatest public health risk due to their epidemic potential and/or insufficient countermeasures against them. The WHO priority diseases list also includes "Disease X" which represents a pathogen currently unknown to cause human disease that can produce a serious international epidemic. Akanocure's approach targets the unknown "Disease X" since it targets host factors hijacked during viral infections of most RNA and even some DNA viruses rather than targeting the virus itself. A virus agnostic approach presents a broad-spectrum strategy that is highly competitive and highly needed, not only to control the current COVID-19 epidemic but to control future unknown viral outbreaks. Akanocure's current efforts are targeted at optimizing its antiviral compound for oral administration and testing its immune-modulatory effects.

The currently available small molecule antivirals against coronaviruses include molnupiravir and nirmatrelvir (Paxlovid). Molnupiravir reduced the risk of hospitalization and death by only 30% for people with mild or moderate COVID-19, the group who can receive the much more effective antibodies. Molnupiravir didn't help patients who had antibodies against the coronavirus from a previous infection or vaccination. Nirmatrelvir, lowered the risk by 90%. However, it is co-administered with ritonavir (to extend its effects), which interacts with many drugs and could therefore limit its use given its tendency to cause life-threatening drug-drug interactions with commonly used medications. Many of the drugs contraindicated with ritonavir are commonly prescribed in older populations at the greatest risk of complications from COVID-19 infection. Obviously, there is a big room for improvement. Neither drug is prescribed for hospitalized patients with advanced disease, representing another room for improvement and a gap that needs to be filled. Akanocure's strategy can target early, as well as late stage infections. Resistance will eventually develop to molnupiravir and nirmatrelvir since they are direct acting antivirals against a virus that mutates very frequently. Akanocure avoids that by targeting the host that is genetically stable and offers the potential to combat the next pandemic against an unknown virus.

Alexander N. Freiberg, PhD, Associate Professor.

Dr. Freiberg is Akanocure's collaborator at the Department of Pathology, UTMB, Galveston. He is the Director of the Robert E. Shope BSL-4 Laboratory, He is also a member of the Center for Biodefense & Emerging Infectious Diseases, and a member of the Sealy Center for Vaccine Development.