

# Strong Effectiveness of NanoViricides Drug Candidates Observed in an Animal Model of Infection by an ACE2-using Human Coronavirus

May 20, 2020 - NanoViricides, Inc. (NYSE American: NNVC) (the "Company") a leader in the development of highly effective antiviral therapies based on a novel nanomedicines platform, announced today that strong effectiveness against infection by an ACE2-utilizing coronavirus in an animal model has been observed for the drug candidates it is developing against SARS-CoV-2 to treat COVID-19 spectrum of diseases. NanoViricides is developing an animal model for coronavirus infection using hCoV-NL63 as a surrogate for SARS-CoV-2, the virus that causes COVID-19 disease. HCoV-NL63 is a circulating human coronavirus that causes a disease that is similar to SARS-CoV-2, but much milder. Both viruses utilize the same cell receptor, namely ACE2, to gain entry into the cell. Because it causes a mild disease, hCoV-NL63 can be used in BSL2 environments, and the Company believes it is a useful surrogate for development of therapeutics against SARS-CoV-2 infection. In this lethal direct-lung-infection model, animals in all groups developed lung disease which later led to multi-organ failures, a clinical pathology resembling that of the SARS-CoV-2. Reduction in loss of body weight at day 7 was used as the primary indicator of drug effectiveness. Rats were infected directly into lungs with lethal amounts of hCoV-NL63 virus particles and then different groups were treated separately with five different nanoviricides drug candidates, remdesivir as a positive control, and the vehicle as a negative control. The treatment was intravenous by tail-vein injection once daily for five days, except in the case of remdesivir wherein it was by tail-vein injection twice daily. Animals treated with the five different nanoviricides showed significantly reduced body weight loss. The body weight loss was only 3.9% for the best nanoviricide candidate, ranging to 11.2% for the potentially least effective one, as compared to 20% in the vehicle-treated control group, in female animals (n=5 in each group). Male animals treated with the same nanoviricides also showed significantly reduced body weight loss. The body weight loss in male animals was 8.0% for the best nanoviricide candidate and ranged up to 10.9% for the potentially least effective one, as compared to 25% in the vehicle-treated control group (n=5 in each group). In comparison, remdesivir treatment led to a body weight loss of 15.2% in females and 18.6% in males in this study (see below). Smaller numbers mean less loss in body weight compared to starting body weight in the group, and indicate greater drug effectiveness. The strong effectiveness of nanoviricide drug candidates in this model is consistent with the effectiveness observed in cell culture studies against infection of both hCoV-NL63, which was used in this study, and hCoV-229E, another circulating coronavirus that uses a distinctly different receptor, namely APN. Thus this study corroborates the previous cell-culture effectiveness reported by the Company and provides confidence to the Company that these nanoviricides drug candidates may be expected to result in a clinical candidate to be pursued in human clinical trials. The Company believes the fact that these nanoviricides anti-coronavirus drug candidates are highly effective against two distinctly different coronaviruses that use different cellular receptors is very significant. Specifically, it provides a rational basis to scientists indicating that even if the SARS-CoV-2 coronavirus mutates, the nanoviricides can be expected to continue to remain effective. Importantly, nanoviricides are designed to act by a novel mechanism of action, trapping the virus particle like the "Venus-fly-trap" flower does for insects. Antibodies, in contrast, only label the virus for other components of the immune system to take care of. It is well known that the immune system is not functioning properly at least in severe COVID-19 patients. The Company believes that these nanoviricides drug candidates are potentially superior to favipiravir, based on cell culture studies and may be superior to remdesivir based on the results of this study, however, a definite conclusion to that effect cannot be drawn. Oral favipiravir and infusion of remdesivir are two anti-viral drugs in clinical trials for the treatment of COVID-19. Prior to filing for human clinical trials, NanoViricides plans on conducting studies to further determine the effectiveness against SARS-CoV-2, perform drug development studies for safety/toxicology, and request a pre-IND Meeting with the US FDA for regulatory guidance. Human coronavirus NL63 (hCoV-NL63) uses the same ACE2 receptor as the SARS-CoV-2 that causes CoVID-19. Both in terms of its clinical pathology, and its receptor usage, it is known to be very similar to SARS-CoV-2, except much milder. Therefore the Company believes hCoV-NL63 is a good surrogate model for therapeutics development against SARS-CoV-2. HCoV-NL63 can be studied in a BSL2 lab whereas SARS-CoV-2 currently requires a BSL3 or BSL4 facility. The striking difference in weight loss between the two sexes in this animal model was remarkable. It has been widely reported that men are more likely to suffer severe infection and fatalities from SARS-CoV-2 than women in the current pandemic. This feature was replicated in our animal model study indicating that biological sex differences are the driver of the differences in the severity of infection by the coronaviruses that utilize the ACE2 receptor. The various receptors used by different coronaviruses appear to fall in the broad family of membrane-associated serine proteases. As a family, they share several structural features. Their substrate specificities are dictated by specific amino acid residues and their positions. However, the coronaviruses do not appear to insert into the specific substrate sites on their receptors as can be broadly deduced from limited, available knowledge of these interactions. NanoViricides believes that this has made it possible for the Company to develop receptor-mimetic virus-binding ligands that have broad-spectrum effectiveness against multiple coronaviruses that use different receptors. HCoV-NL63 is known to cause severe lower respiratory tract infections in young children leading to hospitalization. The symptoms are generally less severe than SARS-CoV-2 but are

similar. In most cases, hCoV-NL63 causes relatively mild disease, often associated with croup, bronchiolitis, and lower respiratory tract disease in children, and is considered to cause some of the common colds in adults. Thus, the clinical manifestation of hCoV-NL63 infection in pediatric patients is similar to that of SARS-CoV-2, although much less severe. SARS-CoV-2 causes clinically similar milder forms of disease in most patients, but moderate to severe disease requiring hospitalizations in about 15-20% of infected persons. These similarities imply that hCoV-NL63 should be a reasonable model virus for antiviral cell culture and animal studies in BSL2 environment in the course of antiviral drug development for SARS-CoV-2.

About NanoViricides NanoViricides, Inc. ([www.nanoviricides.com](http://www.nanoviricides.com)) is a development stage company that is creating special purpose nanomaterials for antiviral therapy. The Company's novel nanoviricide(R) class of drug candidates are designed to specifically attack enveloped virus particles and to dismantle them. Our lead drug candidate is NV-HHV-101 with its first indication as dermal topical cream for the treatment of shingles rash. The Company is also developing drugs against a number of viral diseases including oral and genital Herpes, viral diseases of the eye including EKC and herpes keratitis, H1N1 swine flu, H5N1 bird flu, seasonal Influenza, HIV, Hepatitis C, Rabies, Dengue fever, and Ebola virus, among others. The Company's technology is based on broad, exclusive, sub-licensable, field licenses to drugs developed in these areas from TheraCour Pharma, Inc. The Company does not currently have a license to the coronavirus field, however, TheraCour has not denied any licenses to the Company. The Company typically begins the licensing process only after demonstrating effectiveness of some candidates in optimization stage. This press release contains forward-looking statements that reflect the Company's current expectation regarding future events. Actual events could differ materially and substantially from those projected herein and depend on a number of factors. Certain statements in this release, and other written or oral statements made by NanoViricides, Inc. are "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. You should not place undue reliance on forward-looking statements since they involve known and unknown risks, uncertainties and other factors which are, in some cases, beyond the Company's control and which could, and likely will, materially affect actual results, levels of activity, performance or achievements. The Company assumes no obligation to publicly update or revise these forward-looking statements for any reason, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. Important factors that could cause actual results to differ materially from the company's expectations include, but are not limited to, those factors that are disclosed under the heading "Risk Factors" and elsewhere in documents filed by the company from time to time with the United States Securities and Exchange Commission and other regulatory authorities. Although it is not possible to predict or identify all such factors, they may include the following: demonstration and proof of principle in preclinical trials that a nanoviricide is safe and effective; successful development of our product candidates; our ability to seek and obtain regulatory approvals, including with respect to the indications we are seeking; the successful commercialization of our product candidates; and market acceptance of our products. As with any drug development efforts, there can be no assurance that any of these candidates would show sufficient effectiveness and safety for human clinical development at this time. There can be no assurance that the Company will be successful in establishing the necessary collaborations, although the Company has been successful at establishing necessary collaborations for its drug programs in the past. FDA refers to US Food and Drug Administration. IND application refers to "Investigational New Drug" application. CMC refers to "Chemistry, Manufacture, and Controls".

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