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Nanoviricides (NNVC-AMEX)

NanoViricides Broad Spectrum Technology Represents Potential Paradigm Shift in Viral Therapy…

Research Note

NanoViricides is a biopharmaceutical company developing anti-viral therapeutics based on its proprietary nanoviricide technology. A Phase 1 safety study of the company's lead asset, NV-387, was recently completed and we anticipate results from the study being available in the second half of 2024. A Phase 2 clinical trial in Respiratory Syncytial Virus (RSV) is currently being planned. As opposed to currently available antiviral therapies in which each compound is only active against a unique type of virus, NanoViricides has disclosed preclinical results for NV-387 in multiple viral models that demonstrates the broad-spectrum action of the compound. These results could represent a new paradigm in viral therapy.

Over the past few months, NanoViricides has disclosed positive preclinical results for NV-387 in a number of different viral models. While originally designed as a treatment for COVID-19, the company has additionally reported positive results in RSV, influenza, and pox viruses.

RSV: The company reported results from a direct-lung RSV infection study. Animals treated with vehicle alone survived seven days. Ribavirin therapy, a positive control, resulted in animals surviving 16 days. Animals treated with NV-387 by oral gavage survived 15 days, which was very close to matching the efficacy of ribavirin. NV-387 demonstrated high oral bioavailability in this study on the order of 50%.
In a second RSV study, extended dosing of oral NV-387 was compared with high dose oral ribavirin. Two doses of NV-387 were given on the first day followed by one daily dose for the next nine days. Animals treated with NV-387 showed no lung damage by histopathology at any time points, including at the end of the study. All NV-387-treated animals survived to the end of the 21-day study period. In contrast, animals treated with ribavirin showed progressive lung pathology with moderate levels of inflammation on Day 10, which increased to severe infection with alveolitis and severe pneumonia on Day 13. All ribavirin-treated animals died by Day 14.

Influenza: A lethal lung infection study was performed with Influenza A/H3N2 in which infected mice were treated with NV-387, oseltamivir (Tamiflu®), peramivir (Rapivab®), or baloxavir (Xofluza®). The following table shows the survival of the different cohorts, with NV-387 treatment leading to a survival of 15 days, compared to 10 days for oseltamivir and 11 days for both peramivir and baloxavir. The vehicle treated animals survived eight days.

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Survival Lifespan of Lethally Infected Mice - Lung Infection with Influenza A H3N2			
Treatment	**Survival, Days**	**Increase in Survival, Days**	**Increase in Survival, %**
NV-387, Oral	15	7	88%
Oseltamivir, Oral	10	2	25%
Peramivir, I.V.	11	3	38%
Baloxivir, Oral	11	3	38%
Vehicle	8	0	0%

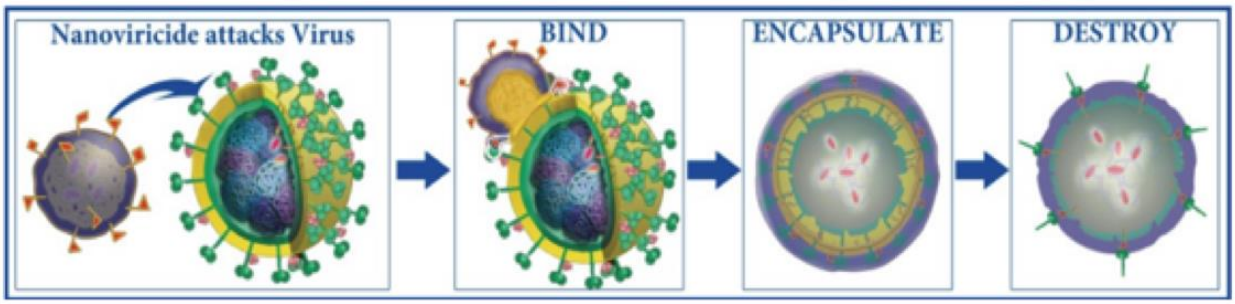
Source: NanoViricides, Inc.

Given the broad-spectrum activity of NV-387 against many different virus families, the activity of the compound against Influenza A/H3N2 is likely indicative of potential activity against most, if not all, influenza A viruses including H5N1 avian influenza.

Mpox/Smallpox: Ectromelia virus is genetically similar to variola virus and thus is used as a model for monkeypox (mpox) and smallpox therapeutic development in mice. NanoViricides studied NV-387 in the ectromelia model and compared it to vehicle, tecovorimat (TPOXX®), and a combination of NV-387 and tecovorimat. The results showed that vehicle-treated mice died in eight days, while treatment with NV-387 or tecovorimat increased the survival to 14 days. The combination of NV-387 and tecovorimat increased survival to 17 days. Tecovorimat is an approved smallpox therapeutic and is stockpiled by the Biomedical Advanced Research and Development Authority under Project BioShield. SIGA Pharmaceuticals announced an original development and procurement contract worth approximately $435 million in 2011, followed by another procurement contract in 2018 upon regulatory approval worth approximately $629 million. Follow on procurement orders of approximately $138 million and $113 million occurred in July 2023 and July 2024, respectively.

Nanoviricide Technology

The ability of NV-387 to show efficacy against a wide range of viruses stems from the company's core nanoviricide™ technology that utilizes molecular mimicry to bind viral particles. A nanoviricide consists of a ligand (small molecule, peptide, or antibody fragment) that mimics the receptor utilized by a virus to gain cellular entry which is covalently attached to a flexible polymer backbone comprised of polyethylene glycol (PEG) and alkyl chains. The PEG forms a hydrophilic shell while also conferring non-immunogenicity. Upon encounter with a target virus, binding occurs between the ligand displayed on the nanoviricide micelle and the viral receptor protein. The micelle then fuses with the lipid-coated surface of the virus through phase-inversion, and "lipid-lipid mixing", a well-studied physicochemical effect. This is shown in the following figure.



Source: Nanoviricides, Inc.

NV-387 mimics the sulfated proteoglycans that are utilized by approximately 90% of pathogenic viruses (e.g., coronaviruses, paramyxoviruses, dengue viruses, herpesviruses, and poxviruses) to enter a cell. The family of sulfated proteoglycans includes heparan sulfate, dermatan sulfate, chondroitin sulfate, and keratan sulfate and are expressed on almost all eukaryotic cells. Since the binding site for those viruses does not change, despite mutations occurring in the virus, it is thought that nanoviricides will not be susceptible to viral mutations that can render other treatments ineffective.

A key distinguishing characteristic of the nanoviricide technology is the fact that they attack the virus outside the cell and can be loaded with antiviral agents to work synergistically inside the cell as well. This is in direct contrast to most other antiviral agents under development that only target the intracellular life cycle of viruses. The company has previously published results showing that encapsulation of remdesivir inside a nanoviricide resulted in increased plasma half-life of the drug and greater efficacy compared to a nanoviricide without remdesivir.

Lastly, a key advantage of the nanoviricide platform is that the drugs can be administered through a variety of different routes, including intravenously, orally, or through inhalation. For NV-387, the company has tested two oral formulations in the Phase 1 trial: oral gummies and an oral syrup. The company has also developed injectable and inhalation formulations for use in hospitalized patients that are expected to follow into clinical development later.

Clinical Plan

NanoViricides has completed a Phase 1 clinical trial of NV-387 that contained both single ascending dose (SAD) and multiple ascending dose (MAD) cohorts of healthy volunteers. In April 2024, the company reported that there were no reported adverse events and that the CRO was in the process of completing the database lock for further statistical analysis. Those results are expected in the second half of 2024.

The company is now focused on determining the spectrum of effectiveness of NV-387 and has initiated discussions with physicians and clinical site investigators in India to design clinical trials to determine its optimum dosage and in what indications it is most effective. If shown to have broad spectrum antiviral activity, NV-387 could be used in a similar manner to how antibiotics are prescribed prior to identification of the pathogenic bacteria when patients present with an unknown viral infection.

More specifically, NanoViricides has initiated the design of a Phase 2 trial of NV-387 in RSV patients. The company has plans to submit a pre-IND application with the U.S. FDA in order to receive feedback on the trial parameters. A Phase 2 trial in adults will occur first, and if successful, a follow-on Phase 2/3 study of RSV-infected hospitalized infants and children would proceed.

The RSV market was approximately $3.9 billion in 2023 and is expected to grow to $11.9 billion in 2030 (EvaluatePharma). Currently, there are three vaccines approved for use in adults 60 years of age and older: Arexvy (which had 2023 revenues of $1.5 billion), Abrysvo (which had 2023 revenues of $890 million), and mRESVIA (which was approved on May 31, 2024). Abrysvo is also approved for pregnant mothers at weeks 32-36 of pregnancy. Beyfortus (2023 revenues of $106 million) is a monoclonal antibody approved to prevent RSV infection in infants younger than 8 months of age or those age 8-19 months who are at increased risk of severe disease. Synagis (2023 revenues of $547 million) is a monoclonal antibody approved to treat severe RSV infection in high-risk children and infants. Lastly, ribavirin is an antiviral nucleoside analog that is conditionally approved to treated individuals infected with RSV at high risk of progressing to severe disease. However, it causes a number of side effects including nausea, vomiting, anemia, and mood changes. There is no other treatment once RSV infection has taken place.

Conclusion

NanoViricides is now a clinical stage company with an exciting, potentially broad-spectrum antiviral asset in NV-387. The preclinical results showing efficacy in different viral models is supportive of the drug's potential utility as a therapeutic against a wide range of viruses. We look forward to the final results from the Phase 1 clinical trial of NV-387 as well as the company's expected timeline for moving it into a Phase 2 trial in RSV and additional indications that will be pursued.

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