Ansun Biopharma, Inc.
www.ansunbiopharma.com

Developing DAS181 for influenza and other infections

Taking a unique approach by targeting the virus host cell, Ansun BioPharma of San Diego, California is developing lead candidate Fludase (DAS181), which has shown potential for the treatment of parainfluenza, influenza and other viruses, including resistant strains.

Viruses are difficult targets for drug developers, who must succeed in blocking viral replication without harming the host cell. Despite important successes, there are no treatments for many common viruses, and antiviral drug resistance is a problem as well. Hospitalized parainfluenza and influenza infections in particular remain a major unmet medical need.

Ansun BioPharma has taken a unique approach to developing an antiviral to treat severe hospitalized parainfluenza, influenza and other infections, sidestepping the virus itself to target the host cell instead. Ansun's lead drug candidate, Fludase (DAS181), removes a host cell-surface component used by parainfluenza virus (PIV), influenza virus (IFV), and other viruses to gain entry into host respiratory cells (**Fig. 1**). In preclinical and clinical studies, DAS181 has shown broad activity against PIV and flu viruses, including resistant strains. On the basis of these promising results, the US Food and Drug Administration (FDA) has granted DAS181 both Fast Track and Breakthrough Therapy designations. According to Ansun CEO Nancy Chang, "We have quietly been developing DAS181 to treat severely ill patients infected with PIV and other respiratory infectious diseases, including influenza, for a number of years. The Breakthrough Therapy designation was an exciting milestone in the clinical development of this potentially lifesaving drug."

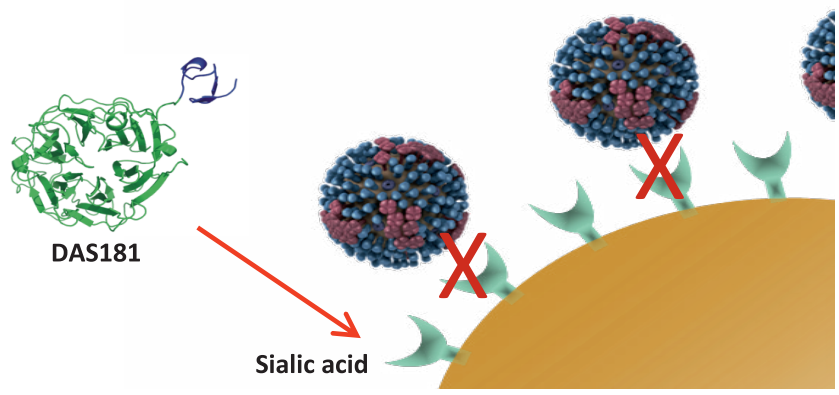

Fig. 1 | DAS181 mechanism of action. DAS181 enzymatically cleaves viral receptors on the host epithelial cell (red X symbols), preventing binding of influenza, parainfluenza, and other viruses.

The parainfluenza challenge

In the US alone, 55,000–200,000 people annually are hospitalized with PIV infections, and another 140,000–700,000 hospitalized patients are infected with flu viruses. Hospitalized and immune-compromised patients are particularly vulnerable. Whereas healthy people can usually resolve PIV infection, in less robust patients, the virus can move unchecked into the lower respiratory tract, where it may prove fatal. Currently, there are no effective treatments for parainfluenza and severe flu infection in hospitalized patients. And although neuraminidase inhibitors are effective against some flu infections, there have been as many as 55,000 flu-related deaths in the US in a single flu season, according to estimates from the US Centers for Disease Control and Prevention.

The broad spectrum challenge

All IFVs infect respiratory epithelial cells by attaching to sialic acid (SA) on host cell-surface receptors. A first-in-class recombinant fusion protein developed in-house by Ansun, DAS181 adheres to the epithelium and cleaves SA from the cell surface, preventing viral entry. DAS181 is delivered as an aerosolized nebulizer formulation, which allows the sialidase to act topically to remove SA at the site of infection. DAS181 has been shown to have potent antiviral activity against all forms of influenza, including pandemic strains such as H1N1 and avian flu. DAS181 is also active against drug-resistant IFV, including strains resistant to Tamiflu (oseltamivir) and Relenza (zanamivir). Asian lineage avian influenza A (H7N9) virus and two additional respiratory viruses that cause serious illness and depend on SA to infect cells, metapneumovirus and enterovirus 68, are also inhibited by DAS181.

Phase 3 clinical trials in sight

Ansun is currently working with the FDA to plan and launch a phase 3 clinical trial of DAS181 in hospitalized patients with PIV infection. The company also intends to conduct further testing of DAS181 in hospitalized flu patients in the future.

At physician request, over 150 patients have been treated with DAS181 under emergency Investigational New Drug (IND) status for compassionate use, including pediatric patients as young as 8 months old. In one independent single-center, single-arm study, 16 patients infected with PIV after hematopoietic stem cell transplant were given DAS181 daily for 5–10 days[1]. Thirteen of the 16 patients (71%) had a clinical response, and 9 of them (56%) showed complete responses.

Virologic data from seven patients showed a reduction in viral load in five patients and functional improvement (increased forced expiratory volume) in four patients after DAS181 treatment. In a preclinical study, DAS181 inhibited the replication of drug-resistant and wild-type (H7N9) influenza A and, when given once daily soon after infection, rescued 100% of lethally infected mice from mortality[2].

Ansun was founded in 2003 and is led by Chang, who also founded Tanox, which was acquired by Genentech. This year Ansun raised $85 million in a Series A financing led by Lilly Asia Ventures and Sinopharm Capital and joined by Lyfe Capital, Yuanming Capital, Matrix Partners, VI Ventures, Joincap Investment, 3E Bioventures, Oceanpine Capital and others.

"The Series A funding we secured this year will allow Ansun to complete its phase 3 study of DAS181 in hospitalized PIV, move forward with plans in hospitalized flu, grow its pipeline of potentially life-saving drugs and bring Ansun to the forefront of drug development in San Diego," stated Yi Shi, of Lilly Asia Ventures who now sits on the Board of Ansun. "We are very excited about the future of Ansun," added Chang.

1. Salvatore, M. et al. *Biol. Blood Marrow Transplant.* **22**, 965–970 (2016).
2. Marjuki, H. et al. *J. Infect. Dis.* **210**, 435–440 (2014).

contact
Mike Havluciyan, Senior VP of Operations
Ansun Biopharma, Inc.
San Diego, CA, USA
Tel: +1-858-452-2631, ext. 186
Email: mhavluciyan@ansunbiopharma.com