N001: an intranasal, host-directed prophylactic antiviral agent

Non-confidential summary

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Objective

Ness Therapeutics (Ness) is developing N001, a virus-agnostic, intranasal, self-administered, host-directed prophylactic; a therapy that will block transmission of all serious respiratory virus infections. Our strategy is to disrupt and move beyond the more traditional approaches of vaccines and pathogen targeted therapeutics.

N001 is a recombinant biologic, formulated to be delivered as a nasal spray. The most effective route of administration for any respiratory infection therapeutic is directly into the respiratory tract - nasal administration that induces a local antiviral state in the upper respiratory tract. N001 is designed to limit initial viral replication at the principal portal of entry, reduce onward transmission and prevent progression to the lower respiratory tract and subsequent systemic disease. N001 is a prophylactic intervention against all serious viral upper respiratory tract infections.

Rationale and unmet need

Recent global experiences with SARS, pandemic influenza H1N1, SARS-CoV-2 and respiratory syncytial virus (RSV), have highlighted a structural gap in pandemic and seasonal preparedness for virus infections. Vaccines remain essential, but each is virus-specific, take time to develop for newly emerging viruses and, although reducing severity of disease, often do not prevent transmission or reinfection. Moreover, as the virus mutates, vaccines, and monoclonal antibodies, become less effective. For newly emerging viruses, there is a window in time for which no vaccine is available. Direct-acting small-molecule antivirals are typically used after infection has occurred, often in a narrow subset of patients and, like vaccines and monoclonal antibodies, may become ineffective as the virus mutates, i.e. drug resistance for pathogen-specific antivirals is inevitable.

A complementary, host-directed prophylactic that can be deployed regardless of the virus type and its potential for antigenic drift, would address several of these limitations. N001 is designed precisely for this role: a broad-spectrum, virus-agnostic, host-directed prophylactic, that can be used in seasonal outbreaks and in the early phases of epidemics and pandemics, without the need for pathogen-specific reformulation.

N001 can be stockpiled or manufactured at scale and can be administered alone or in addition to vaccines and antivirals, to enhance viral clearance and blunt an outbreak.

Priority use cases include young children and the elderly, individuals who are immunocompromised and frontline health care workers and first responders.

Scientific foundation

The N001 program is grounded in extensive human preclinical and clinical studies, that targeted SARS, pandemic H1N1 and avian H5N1 influenzas, and SARS-CoV-2. These studies

demonstrated accelerated viral clearance, reduced lung pathology, favourable modulation of host responses and an excellent tolerability profile, including in severe disease settings. More specifically, a randomized clinical trial showed reduced transmission of SARS CoV-2 from an infected individual to exposed, uninfected household contacts, most pronounced when the infected individual had a high viral burden. These proof of principle data clearly demonstrated activation of a host immune response to protect from infection and block transmission. Simply put, to stop an outbreak, epidemic or pandemic, blocking transmission is an absolute requirement. With the development of N001 we will transform therapeutic interventions for viral outbreaks, a paradigm shift away from treatment after infection, that will complement vaccine strategies, and provide a virus -agnostic, deployable intervention.

Product concept and intended use

N001 is being developed as a multidose intranasal spray that can be self-administered. Key attributes are:

- Host-directed, virus-agnostic mechanism based on induction of an antiviral state in the nasal mucosa
- Local delivery to the upper respiratory tract, where infection is initiated and from which transmission occurs
- Favourable safety and tolerability expectations informed by prior clinical experience with the underlying biologic
- Compatibility with repeated use during high-risk periods, e.g. seasonal outbreaks, local outbreaks, or in specific close exposure settings: hospital wards, clinics and long-term care facilities

The intended positioning is as a broadly deployable prophylactic that reduces the incidence and severity of upper respiratory infections and the associated burden on healthcare systems, while also providing a practical tool for early outbreak control.

Development status

Ness is now translating this concept into a clinically and commercially viable product:

- The N001 gene has been cloned and expressed in bacterial hosts that are suitable for scalable biologics manufacture. Laboratory-scale upstream and downstream processes have been established, and purified N001 has demonstrated robust antiviral bioactivity in vitro and in relevant cellular systems.
- IND-enabling development is underway at the National Research Council Canada. Activities include generation of N001 drug substance, advanced analytical characterisation, formulation development, and toxicology and pharmacokinetic studies in support of first-in-human use.
- Ness is developing a proprietary intranasal formulation for N001 based on biodegradable materials in a user-friendly multidose nasal spray device. This combination is designed to enhance stability, enable reproducible delivery to the nasal mucosa and support large-scale deployment.

- Planning is in progress for a first-in-human clinical study in Europe that will characterise the safety, pharmacokinetics and pharmacodynamic activity of intranasal N001 in a population representative of real-world respiratory risk.

Parallel work is being conducted to establish immunophenotypic readouts/biomarkers of immune-response signatures, to characterize how N001 shapes mucosal and systemic responses and to inform indication and population prioritisation.

Ness is advancing N001 through first-in-human evaluation and into targeted Phase 2 studies together with a focused group of academic scientists and clinicians as well as industrial collaborators. Potential new collaborations are explored where there is clear scientific and strategic alignment with the N001 programme, with partnership decisions remaining at the discretion of Ness.