RIGImmune Announces Multiple Oral Presentations for Intranasal RIG-101 at European Respiratory Society Congress 2024

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RIGImmune Inc. →
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Pre-clinical studies for intranasal RIG-101, a first in class RIG-I agonist, demonstrate potent local innate immune stimulation and pan-viral activity against human rhinovirus, influenza and RSV infections.

RIG-101 is in development for the pan-viral prevention of RNA virus transmission in asthma patients to inhibit seasonal exacerbations.

RIG-101 intranasal (IN) is on track to enter first in human trials in mid-2025.

Farmington, CT, September 9, 2024 – RIGImmune Inc., a biopharmaceutical research company developing a new class of RNA therapeutics, today announced three oral presentations demonstrating the viral prevention effects of intranasal RIG-101, their lead product development candidate, at the

European Respiratory Society (ERS) Congress 2024 in Vienna, Austria. The three oral presentations highlight the impressive results from pre-clinical studies demonstrating that the company's first in class RIG-I agonist has the ability to rapidly and substantially reduce viral loads by inducing innate immune responses when delivered directly to the respiratory tract. Intranasal RIG-101 is formulated with the company's novel NEED™ (Nano-Emulsion Enhanced Delivery) platform, a complex designed to deliver a wide range of RNA payloads without the use of lipid nanoparticle encapsulation. The results from these studies and other company experiments demonstrate the potential for RIG-101 to inhibit the transmission of an RNA virus from an infected person to a non-infected individual and could significantly reduce viral infection-related respiratory complications in at-risk patient populations, including the immune-compromised and those with chronic respiratory diseases such as asthma and COPD.

"While the nose is an obvious passageway to leverage for infectious disease prevention, inefficient uptake of previous intranasal RNA therapeutics by the nasal epithelial cells has been a barrier to infection prevention," said the senior author of all three studies, Kazuhiro Ito, Ph.D., principal research fellow of Respiratory Molecular Pharmacology in Genomic and Environmental Medicine Section in National Heart and Lung Institute (NHLI) in the Faculty of Medicine of Imperial College London, and vice president of biology at RIGImmune. "Our study results show that RIG-101, formulated with our proprietary NEED™ technology can induce efficient uptake into the epithelium and is uniquely optimized to activate the innate immune system to fight viral respiratory diseases with local intranasal administration. The NEED™ platform allows us to effectively deliver RNA therapeutic payloads directly to the upper and lower respiratory tract and avoid the use of LNPs, which can damage the respiratory system when given locally."

“We’re excited with the study results presented by Dr. Ito at the 2024 European Respiratory Society. The data from these studies and other work conducted by RIGImmune demonstrate potent pan-viral activity for RIG-101 formulated with our NEED™ technology platform,” said Susan Sobolov, Ph.D., president of RIGImmune. “We have designed NEED™ to enable targeted delivery of a broad range of RNA therapeutics that aligns with the body’s own biological pathways, thereby minimizing toxicity risks. By validating RIG-101 in our NEEDTM formulation technology in these pre-clinical systems that have demonstrated translation to the clinical setting, we are further committed to advancing RIG-101 intranasal to our first-in-human studies in mid-2025.”

Description of RIG-101 Study Results Presented at European Respiratory Society Sept 7th – 11th:

Title: Pan-antiviral effects of RIG-I agonists (RIG-101) against respiratory syncytial virus and human rhinovirus in nasal epithelium in vitro and mice in vivo

Overview
Prophylactic intranasal RIG-101 demonstrates potent antiviral activities against human rhinovirus (HRV) and respiratory syncytial virus (RSV), potentially preventing respiratory virus-induced asthma and similar respiratory disorders.

Details
This study, led by Leah Daly of Imperial College London, showed that RIG-101 was able to induce interferon signaling in fully differentiated human nasal

epithelium when delivered the day-prior and day-of viral exposure at apical site in air-liquid interface (ALI).

In vivo testing demonstrated statistically significant reductions in HRV1B viral load and neutrophilia compared to pleconaril. Intranasal RIG-101 NEEDTM (2mg/ml) was administered 4 and 1 day prior to exposure, with evaluations one day following exposure, and oral pleconaril (200 mg/kg) was administered up to one day prior to viral exposure.

Title: Effects of an anti-viral interferon booster, RIG-I agonist (RIG-101), on influenza infection in vitro and in vivo

Overview
Prophylactic intranasal RIG-101 offers signs of viral prevention efficacy against influenza infection, and demonstrated increased immune response

Details
In an oral presentation, researchers, led by Hugo Ombredane, Ph.D. student at Imperial College London, demonstrated that delivering intranasal RIG-101 prophylactically offered significant induction of type I/III interferon signalling and potent antiviral effects against influenza with antiviral effect comparable or superior to oseltamivir in both in vivo and in vitro models.

RIG-101 significantly reduced viral load in vivo and in vitro, as well as strongly induced CXCL10, a surrogate marker of antiviral interferon production in vitro and prevented neutrophil accumulation, a sign of inflammation, in the nasal lavage in vivo.

For this study, RIG-101 was delivered 4 days and 1 day prior to viral exposure in vitro and 3 days, 1 day and 1 hour prior to viral exposure in vivo, and evaluations were conducted 48 hours post-viral exposure in vitro and 1-5 days post-viral exposure in vivo.

Title: Adjutancy effects of a RIG-I agonist (RIG101) on H1N1 HA antigen intranasally vaccinated mice and human nasal epithelium/PBMCs co-culture

Overview
Adding prophylactic intranasal RIG-101 to the recombinant seasonal influenza hemagglutinin (rHA) vaccine more effectively reduced viral load and inflammation associated with the H1N1 HA subtype of influenza.

Details
RIG-101 combined with the recombinant seasonal influenza hemagglutinin (rHA) vaccine not only reduced viral load and inflammation associated with H1N1 HA, but also prevented virus-induced body weight loss compared with both HA antigen vaccination alone and the HA antigen vaccine plus CPG-ODN vaccine addition in a preclinical study led by Dr. Shyreen Hassibi of Imperial College London.

An in vitro study involved peripheral blood mononuclear cells (PBMCs), which may include lymphocytes monocytes, natural killer cells (NK cells) and dendritic cells, cultured from the nasal cavity, and found that RIG-101 combined with H1N1 HA vaccination clearly enhanced the body's natural production of immunogobulin M (IgM) antibodies, the first line of defence of the adaptive immune system, compared with H1N1 HA vaccination alone.

Presentation e-posters may be accessed on the Company Presentations page under the Corporate News section of the RIGImmune website as well as the European Respiratory Society Congress website.

About RIGImmune

RIGImmune is a biopharmaceutical research company focused on the development of innovative RNA therapeutics to prevent or treat serious respiratory diseases with high unmet clinical needs. The company was co-founded by the prominent scientists, Drs. Akiko Iwasaki and Anna Pyle from Yale University, to advance the development of a novel class of oligonucleotides called stem-loop RNA therapeutics or "SLRs." These SLRs were discovered in Dr. Pyle's laboratory at Yale. In 2022, RIGImmune combined with a UK-based development company named SubIntro to develop non-lipid nanoparticle formulations for the effective delivery of a broad set of nucleic acid payloads directly to the respiratory tract. SubIntro was co-founded by the prominent research scientists and successful respiratory drug and formulation developers, Drs. Garth Rapeport, Kazuhiro Ito, and Jag Shur.

RIGImmune's lead product development candidate is RIG-101, a stem loop RNA therapeutic that targets the RIG-I pathway to enhance the innate immune response against viral respiratory diseases. RIGImmune's second product development candidate is RIG-301, an mRNA formulated with the NEED™ technology, targeting the CFTR mutation in cystic fibrosis patients. RIGImmune has internally developed a proprietary nano-emulsion delivery technology platform named NEED™ to effectively deliver RNA compounds without the need for lipid nanoparticle encapsulation.

About RIG-101

RIG-101 is a potent agonist of RIG-I, which results in the induction of the interferon pathway in the respiratory epithelium when administered locally. RIG-101 is formulated with the company's NEED™ (Nano-Emulsion Enhanced Delivery) technology and will enter a Phase 1/2a clinical program in mid-2025 for the prevention of seasonal viral exacerbations of asthma. RIGImmune is developing RIG-101 for delivery by multiple routes of administration, including intranasal (IN), a solution for inhalation for lower respiratory tract delivery, intra-muscular, and subcutaneous. In the first clinical program for RIG-101, the product development candidate will be administered by the intranasal route for delivery directly to nasal epithelium. Extensive prior research by noted investigators has shown delivery directly to the nasal epithelium can be critical for comprehensive protection from a broad range of respiratory viruses.

About NEED™ (Nano-Emulsion Enhanced Delivery)

NEED™ is a non-lipid nanoparticle (LNP) formulation platform developed by RIGImmune to effectively deliver RNA directly to the respiratory mucosa and avoid the limitations and potential toxicity concerns associated with LNP delivery systems. The principal novelty of the NEED™ formulation technology is the ability to transform surfactants and natural fatty acids into a proprietary nano-emulsion complex that encapsulates a nucleic acid and protects the payload while controlling particle size and charge, and facilitates intracellular uptake when administered directly to the respiratory epithelium. The first clinical presentation of the NEED™ delivery platform will be an aqueous formulation for the intranasal delivery of RIG-101 to the upper respiratory tract. RIGImmune has shown that NEED™ can also be administered by multiple routes, including a solution for inhalation to the lower respiratory

tract, subcutaneous, and intra-muscular. Initial research conducted by the company has shown the NEED™ delivery platform technology could be compatible and effective with a diverse range of RNA and DNA therapeutics.

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