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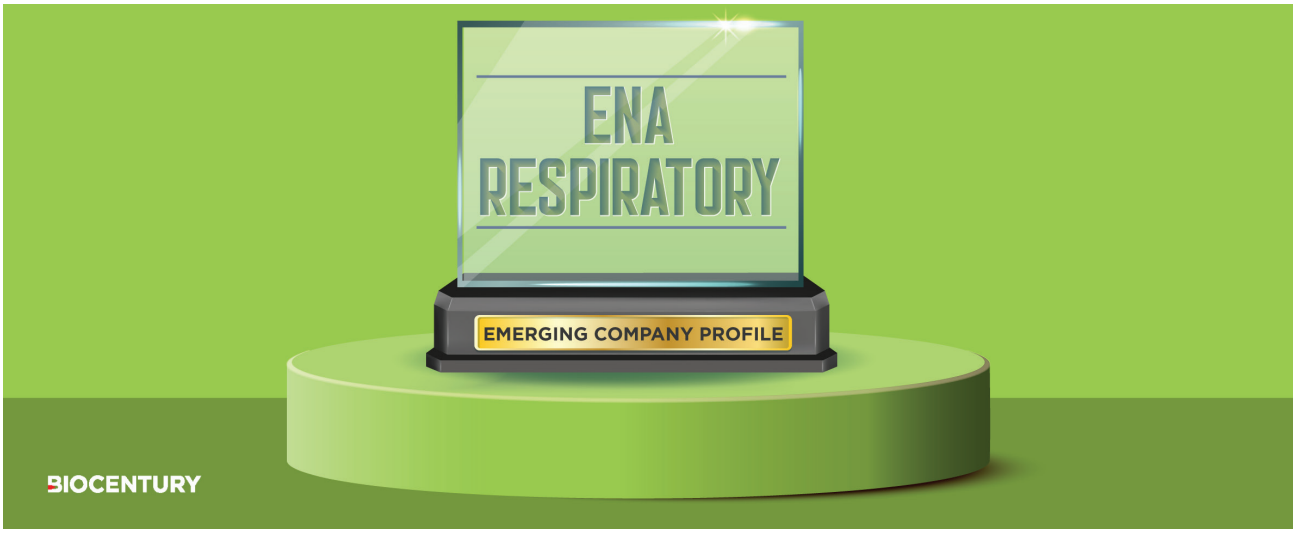
EMERGING COMPANY PROFILE | REPRINT FROM JAN. 5, 2026

ENA Respiratory: Boosting prophylactic immunity with a pan-viral nasal spray

BY LINDSAY MARTIN, BIOPHARMA ANALYST



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With a prophylactic, immune-priming nasal spray in the clinic, Melbourne-based ENA Respiratory believes it can reduce the global burden of airway infections through technology that is virus-agnostic, shelf-stable, and injection-free.

"It's not for any specific virus — that's the beauty of it," ENA Respiratory Pty. Ltd. Managing Director and CEO Christophe Demaison told BioCentury.

ENA Respiratory has launched a Phase II study of its dual TLR2 and TLR6 agonist INNA-051, with the goal of stopping viral upper respiratory infections — including SARS-CoV-2, influenza, and rhinovirus — before they take hold in epithelial cells lining the throat and nasal cavity.

Since becoming an independent company in 2020, ENA Respiratory has raised $47.1 million in venture funds, including an October $22.4 million series B round that included new investors Gates Foundation, Flu Lab, and Stoic Venture Capital, as well as founding investors Brandon Capital and Uniseed.

Although some upper respiratory viruses have available vaccines, viral respiratory infections remain a huge burden to global health, especially for at-risk populations like children and the elderly. The company will first target people who are at risk of complications, with a high risk of being hospitalized, including patients with lung, kidney, heart, and metabolic diseases.

INNA-051 was initially discovered in 2012 by a group led by David Jackson at the University of Melbourne. In 2016, Jackson and Demaison co-founded Innavac Pty. Ltd., renamed to ENA Therapeutics Pty. Ltd. in 2018, with the initial goal of using TLR agonists to create vaccine adjuvants. But during the COVID-19 pandemic, they showed the molecule was active on its own as a prophylactic agent in a ferret model. Two years later, with investors interested, Demaison spun out ENA Respiratory as its own company.

TLR2 is highly expressed on the nasal epithelium, and its natural ligand is a lipid with a peptide attached. Designed to mimic the natural ligand while remaining stable in solution and confined to the nasal passage, INNA-051 is a small molecule analog of the decades-old TLR2/6 agonist Pam2Cys, a diacylated lipopeptide that selectively binds a hydrophobic pocket of TLR2 and forms a heterodimer with TLR6.

In a February Antiviral Research study, ENA Respiratory described the development of INNA-051, with modifications including an optimized polyethylene glycol moiety that enhanced the compound's aqueous solubility while minimizing systemic and lung exposure, which has historically been a driver of toxicity for TLR agonists.

"One of the advantages of the molecule INNA-051 is that it doesn't absorb. It's a very local effect," said Demaison. He added that because INNA-051 is a prophylactic treatment, it's especially important to avoid the flu-like symptoms that are common side effects of TLR agonist therapies, which will be less acceptable to healthy individuals.

Upon binding, the small molecule activates the MyD88 signaling pathway, which upregulates expression of antiviral Type III interferons by epithelial cells. These cytokines are also less prone to inducing flu-like symptoms than the Type I interferons induced by agonists of more commonly targeted TLRs, such as TLR9 .

Moreover, unlike most vaccines and adjuvants that require refrigeration, ENA Respiratory's small molecule is modified to be stable in solution, and it's made as a shelf-stable powder that lasts up to two years.

Immune priming happens in "as little as a few hours, lasting up to seven days," said Demaison. With an already boosted immune system, viral clearance occurs faster and shortens the time of infection.

In Phase I influenza challenge studies, patients treated with INNA-051 two and four days before infection with H3N2 recovered 26 hours faster than patients receiving the placebo.

With a fresh cash infusion, the company is now advancing INNA-051 into Phase II trials designed to measure prevention of natural infections. In the POSITS Phase IIa study, up to 1,100 healthy adults will be treated with the nasal spray or placebo once weekly as a prophylactic measure during the North American respiratory virus season, beginning in December, and followed for signs of respiratory illness.

Other companies aiming to tackle multiple viruses via a single nasal spray include Dutch biotech Leyden Laboratories B.V., which has raised over $300 million since its founding in 2020. The company's CR9114 is a pan-influenza prophylactic antibody licensed from Johnson & Johnson (NYSE:JNJ). The antibody, which is delivered via nasal spray, is in Phase II testing. It was described in an April Scientific Reports paper.

Competitors with host-targeting, virus-agnostic agents include Pulmotect Inc., whose inhaled peptide PUL-042 targets TLR2, TLR6, and TLR9 in lung epithelial cells. PUL-042 is in Phase II testing to treat parainfluenza virus (PIV), human metapneumovirus (hMPV), or respiratory syncytial virus (RSV) infections.

According to BioCentury's BCIQ database, INNA-051 is the only infectious disease product in company pipelines that selectively binds TLR2/6 while excluding TLR9, thus reducing the potential for flu-like symptoms and cytokine storms induced via the Type I interferon response.

After ENA Respiratory spun out of ENA Therapeutics, the parent company was renamed Axelia Oncology Pty. Ltd., with a focus on development of small molecule TLR2/6 agonist AXA-042. It is in Phase I trials for advanced solid tumors.

COMPANY PROFILE

ENA Respiratory Pty. Ltd.

Melbourne, Australia

Technology: TLR2/6 agonist that prevents viral upper respiratory infections

Origin of technology: University of Melbourne

Disease focus: Infectious

Clinical status: Phase II

Founded: 2020 by Christophe Demaison

Academic collaborators: University of Melbourne

Corporate partners: JPEO-CBRND, COPD Foundation, Blue Knight

Number of employees: 4

Funds raised: $47.1 million

Investors: Gates Foundation, Brandon Capital, Flu Lab, Uniseed, Stoic Venture Capital

CEO: Christophe Demaison

Issued Patents: Undisclosed

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