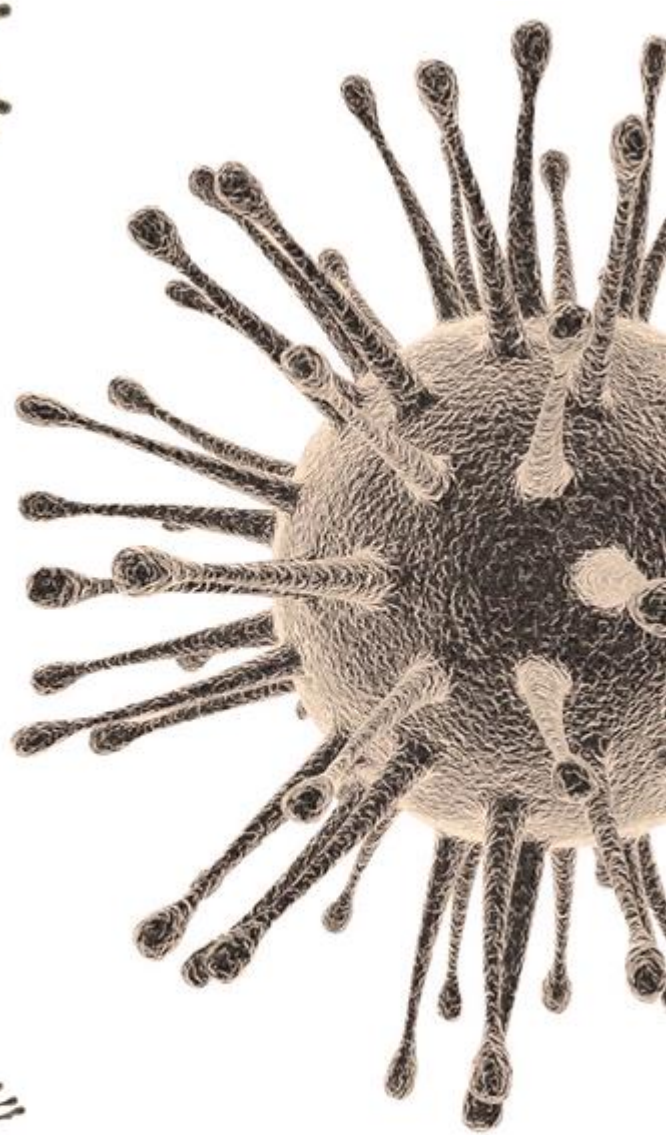
Development of a Novel Prophylactic Immune Enhancer for Respiratory Viral Infections



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From Lab to Line: The Military`s Role in Advancing Infectious Disease Countermeasures
Aug 4 2026 MHSRS-26-3838

Disclosures

Name & Credentials	Role	Commercial Interest / Company	Nature of Relationship
Ruth Tal-Singer, PhD	Presenter/ Faculty	- ENA Respiratory - AstraZeneca, Boehringer Ingelheim, GSK, Sanofi, Janssen, Roche, Renovion, Samay Health, Global Skin - GSK - Global Allergy and Airways Patient Platform	Independent consultant, non-exercised share options Independent consultant Retiree (pension) Research consultant
Courtney Crim, MD	Clinical	- ENA Respiratory - Aer Therapeutics - Chiesi USA, SR One, Fairmont Funds, COPD Foundation, Genetech, Parion Sciences - GSK	Independent consultant, non-exercised share options Independent consultant, non-exercised share options Independent consultant Retiree (pension/non-exercised shares)
Wai Kwan Chung	Program Manager	N/A	CPE CBRND JPM CBRN Medical Funding Agency
Catherine M. Berjohn, MD, MPH	Investigator	N/A	
Anna Stein, MD	Associate Investigator	N/A	
Trevor Wellington, MD	Independent physician, Safety Review Committee	N/A	
Christophe Demaison, PhD		ENA Respiratory	Employee, non-exercised share options

Viral Respiratory Infections Cause Substantial Morbidity and Mortality

Especially during the winter months

Burden estimates [Oct 2024 – May 2025]#

Flu, COVID & RSV - US only

27 - 47 million outpatient Visits

Flu: 21 – 37 million
COVID: 2.3 – 3.8 million
RSV: 3.6 – 6.5 million

1.1 - 2 million Hospitalizations

Flu: 610,000 – 1.3 million
COVID: 270,000 – 430,000
RSV: 190,000 – 350,000

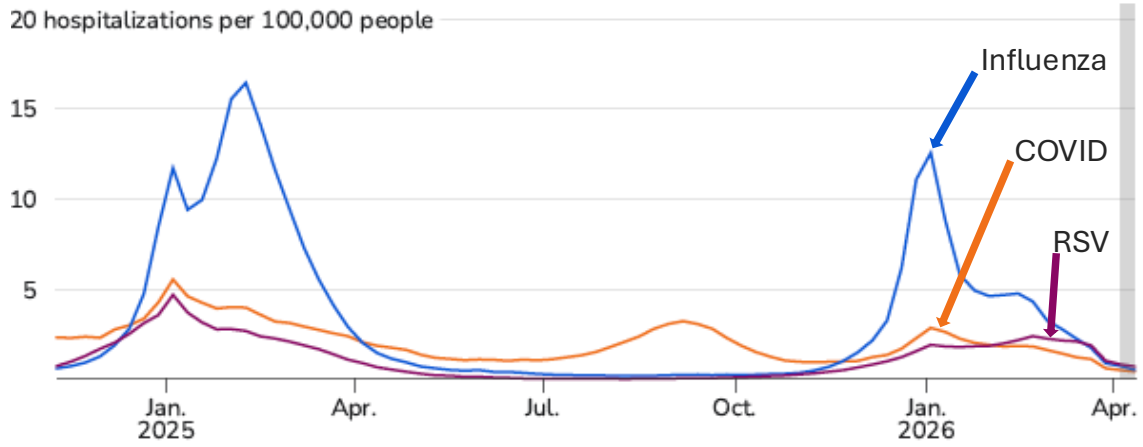
68,000 – 200,000 Deaths

Flu: 27,000 – 130,000
COVID: 31,000 – 50,000
RSV: 10,000 – 23,000

Estimates derived from CDC surveillance-adjusted seasonal burden models

Weekly Hospitalization Rates due to VRIs in the USA

Data from CDC's National Healthcare Safety Network



20 hospitalisations per 100,000 people correspond to over 65,000 hospitalizations per week
(about 5% of total hospitalizations)

https://www.cdc.gov/respiratory-viruses/data/illness-severity.html

Other Viral Respiratory Infections Drive Major Unmet Need

Rhinovirus

- One of the most common circulating respiratory viruses
- Primary trigger of asthma & COPD exacerbations
- Significant morbidity and mortality in older adults
- **No licensed vaccines or antivirals**

Morelli et al. Respiratory Research (2025) 26:120

Human metapneumovirus

- Causes severe respiratory disease in infants & older adults
- Hospitalizations burden overlaps with RSV in ≥65 years
- **No licensed vaccines or prophylaxis**

Monto et al. J Infect Dis. (2025) 231(3):795-804

Viral Acute Respiratory Infections (ARI): a leading cause of active-duty military sick days, including trainees

- NYT **June 18, 2026** "A major **flu outbreak** has sickened nearly 160 troops at Lackland Air Force Base in Texas ….. The outbreak at the base in San Antonio raced through an Air Force Basic Military Training wing, where new recruits sleep on bunk beds in open bays and share meals at large communal tables."

Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Decreased Self-reported Physical Fitness Following SARS-CoV-2 Infection and the Impact of Vaccine Boosters in a Cohort Study

Stephanie A. Richard,[1,2,*] Ann I. Scher,[3] Jennifer Rusiecki,[3] Celia Byrne,[3] Catherine M. Berjohn,[1,3,4] Anthony C. Fries,[5] Tahaniyat Lalani,[1,2,6] Alfred G. Smith,[6] Rupal M. Mody,[7] Anuradha Ganesan,[1,2,8] Nikhil Huprikar,[3,8] Rhonda E. Colombo,[1,2,3,9] Christopher J. Colombo,[3,9] Christina Schofield,[9] David A. Lindholm,[3,10] Katrin Mende,[1,2,10] Michael J. Morris,[10] Milissa U. Jones,[11] Ryan Flanagan,[11] Derek T. Larson,[3,4,12] Evan C. Ewers,[3,12] Samantha E. Bazan,[13] David Saunders,[3] Ryan C. Maves,[14] Jeffrey Livezey,[15] Carlos J. Maldonado,[16] Margaret Sanchez Edwards,[1,2] Julia S. Rozman,[1,2] Robert J. O'Connell,[1] Mark P. Simons,[1] David R. Tribble,[1] Brian K. Agan,[1,2] Timothy H. Burgess,[1] and Simon D. Pollett[1,2,*]; the EPICC COVID-19 Cohort Study Group

" Participants with a history of SARS-CoV-2 infection were **more likely to report difficulties exercising and with daily activities**, as well as decreased FT scores, and these limitations **persisted in some participants for 6 months**. This finding was noted even after adjustment for potential confounding variables and even though most of these cases **(97.5%) had a relatively mild initial COVID-19 illness**."

Richard SA, Scher AI, Rusiecki J, et al. Decreased Self-reported Physical Fitness Following SARS-CoV-2 Infection and the Impact of Vaccine Boosters in a Cohort Study. *Open Forum Infect Dis*. 2023;10(12):ofad579. Published 2023 Nov 17. doi:10.1093/ofid/ofad579

ARI at the US Naval Academy Plebe Summer

"USNA Plebe Summer 2023 was characterized by substantive ARI attack rates due to a diverse array of viruses, relatively frequent codetections, and significant training days lost."

Most common viruses

Influenza, adenovirus, rhinoviruses/enterovirus, PIV (55% of PIV were part of a codetection), HMV, coronavirus (SC2)

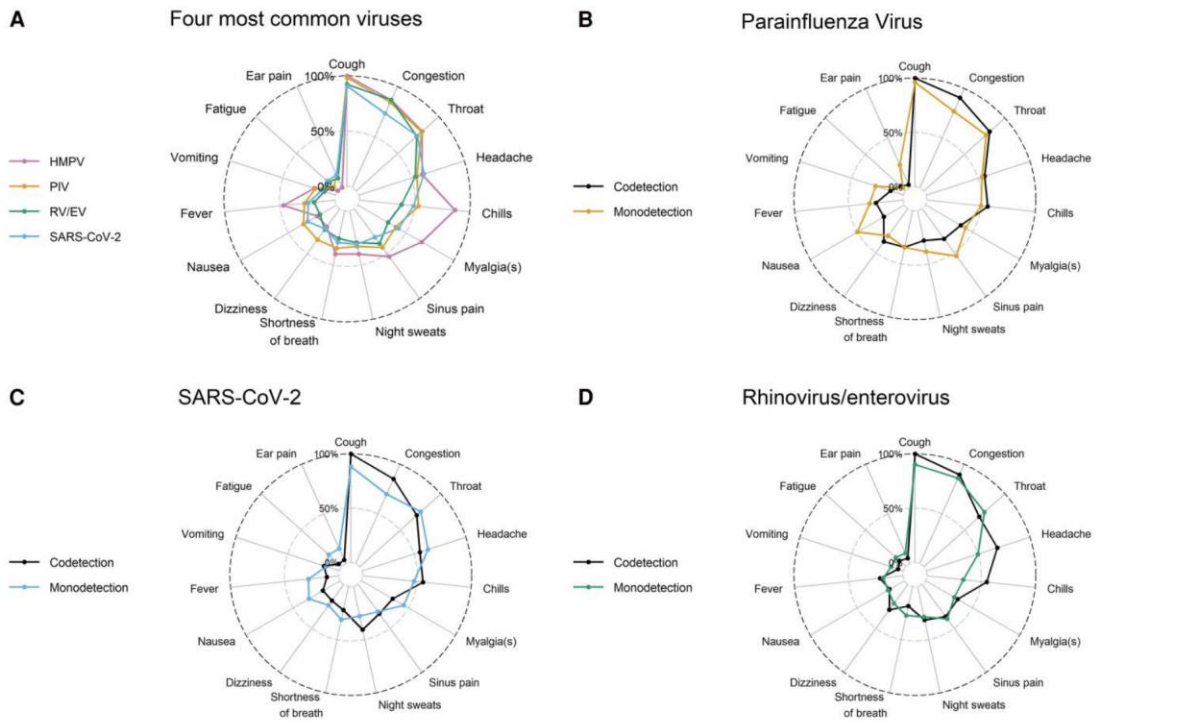


Figure 1. (*A*) The graphs depict the 15 most common respiratory infection symptoms, sorted by frequency (most common symptom is at the top and decreases as you move clockwise around the circle). The points indicate the percentage of cases for which each symptom was documented by respiratory virus, for the 4 most commonly detected viruses, including codetections. (*B-D*) Comparison of symptoms by mono-detection and codetection: *B*, parainfluenza; *C*, SARS-CoV-2; *D*, rhinovirus/enterovirus. Abbreviations: HMPV, human metapneumovirus; PIV, parainfluenza virus; RV/EV, rhinovirus/enterovirus.

Hone E, Richard SA, Schmidt K, et al**. The Molecular Epidemiology and Congregate Transmission Dynamics of Medically Attended Acute Respiratory Infections at the United States Naval Academy During Plebe Summer.** *Open Forum Infect Dis*. 2026;13(2):ofag036..
doi:10.1093/ofid/ofag036Hone E, Richard SA, Schmidt K, et al. The Molecular Epidemiology and Congregate Transmission Dynamics of Medically Attended Acute Respiratory Infections at the United States Naval Academy During Plebe Summer. *Open Forum Infect Dis*. 2026;13(2):ofag036. Published 2026 Jan 30. doi:10.1093/ofid/ofag036

Current Treatment Options Have Limitations

- **Antivirals & vaccines** are only available against a **limited number of respiratory viruses,** and are virus-specific
- **Antivirals** are **largely ineffective** against viral infections once symptoms begin
- **Vaccines** have **relatively low efficacy** against circulating viruses

41-55% Seasonal Influenza Vaccine Effectiveness against Hospitalisations - adults ≥18 years [1]

1: CDC / Morbidity and Mortality Weekly Reports- February 27, 2025

Candidate drug in development:

First-in-Class Intranasal TLR2/6 Agonist Therapy to Minimize the Impact of Viral Respiratory Infections and to Reduce the Burden on the Healthcare System

Novel Mechanism of Action

- Boost the body's natural host defense at the initial site of infection
- Effective against multiple common respiratory viruses

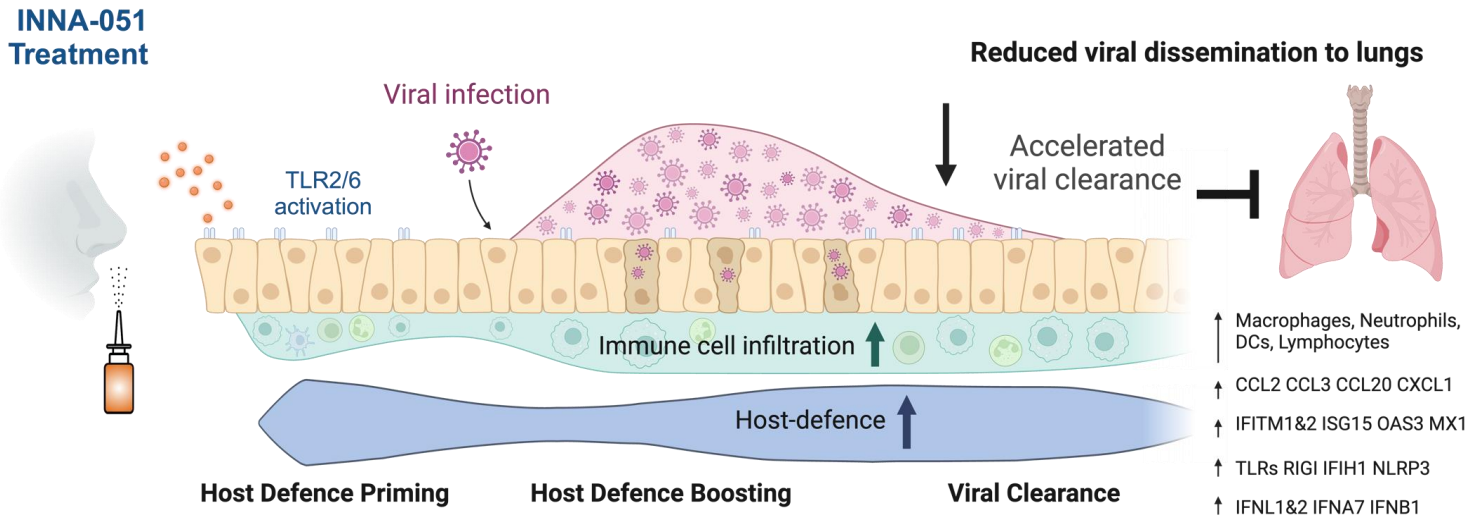
Cost-effective Manufacture & Storage, with Convenient Weekly Administration

- Nasal administration / "needle-free"
- Weekly administration
- Distribution & storage at room temp.
- Localized effect, with no systemic exposure, supporting prophylaxis use

Mechanism of Action

Host Defense Boosting Agent (Small Molecule TLR-2/6 Agonist)

Mechanism of Action



From Mercuri, Francesca A et al. "Discovery and development of INNA-051, a TLR2/6 agonist for the prevention of complications resulting from viral respiratory infections." Antiviral research vol. 234 (2025)

Toll-like receptor 2 (TLR2): cell surface, pathogen-sensing receptor, expressed by nasal epithelial cells[1] and innate immune cells, and involved in stimulating host defences and viral clearance [2-4]

- Host defense stimulation
- Type-1 & -3 IFNs stimulation
- Localized effect - no systemic exposure
- Accelerate viral clearance
- Reduced viral dissemination
- MOA complementary to vaccines

References:
1. Tongeren et al. Clin Transl Allergy (2015);
2. Girkin et al. Eur Respir Rev. (2022);
3. Mercuri et al. ERJ Open Res (2024);
4. Deliyannis et al. JCI Insight (2021) ;
5: Mifsud et al. Frontiers in Immunology (2015)

Pandemic Preparedness Potential

Occupational Risk Populations

US alone
37 million

Age 18-59 (~70%*)	Age 60+ (~30%*)
25.8M	11.2M

- Healthcare workers
- First responders
- Service members
- Educators
- Nursing home residents
- Other frontline workers

*Syneos Data Analysis for Company

Company Support from US Government Organizations

JPM CBRND MEDICAL $16m Contract

Supporting
Clinical & CMC Activities

BLUE KNIGHT™ Alumni Company

BLUE KNIGHT™ Alumni Company

CRADA: Naval Medical Research Command

U.S. GOVERNMENT CONTRACT HISTORY

Defense Funding Timeline

CONTRACT 1 — DoD OTA | HQ08452390003
Dec 2022 – Sep 2025 · Total value: $11,314,524

Dec 2022 — BASE AWARD: OTA Executed

$4,380,000

- Preclinical, manufacturing & regulatory workstreams

Jul 2023 — Scope Expansion

+$3,800,000 → $8,180,000

- Subchronic Toxicology Program

Aug 2024 — Clinical Options Exercised

+$3,134,524 → $11,314,524

- Clinical Study

CONTRACT 2 — DoD OTA | W911SR2530001
Oct 2025 – Dec 2026 · Total value: $5,000,000

Sep 2025 — OTA Executed

$5,000,000

- Phase 2a Part B community trial

Feb 2026 — Clinical Options Exercised

Full $5,000,000 reobligated with revised schedule

$4,380,000	+$3,800,000	+$3,134,524	$5,000,000	$16,314,524
DIU Base Award · Dec 2022	DIU Mod P00002 · Jul 2023	DIU Mod P00003 · Aug 2024	Army Award · Sep 2025	TOTAL COMMITTED

Extensive Data package available for Drug Candidate

Preclinical

Influenza studies

Rhinovirus studies

SARS-CoV2 studies

INNA-051 selection

IND-enabling pharmacology studies

Boost host defence pathways *(incl in asthma human cell line model)*

Accelerates viral clearance

Prevent viral dissemination

Phase 1 & Flu-challenge Phase 2a

Liquid Formulation

Safety & Tolerability

Established in adults (18 - 55 & >60 years)

Proof of Pharmacology

Boosts nasal host defences (incl. IFNλ & α)

Accelerates viral clearance

Dry Powder & Manufacture Process Development

CMC

Drug product with >2y RT shelf life

Particle size profile minimising lung deposition

CMC supporting late-stage clinical studies

3-Month Toxicology Studies

Dry Powder Formulation

Toxicology in NHPs

No dose-limiting findings

Supporting 3-months seasonal dosing in humans

Phase 1b

Dry Powder Formulation

HVT-02

IND approved
June 2024

Safety & Tolerability of the Dry Powder Formulation

Adults aged 18 - 45 & >60 years

Confirm safety & tolerability of the dry powder formulation

Stimulates nasal host defence pathways

Phase 1b

Dry Powder Formulation

HVT-03

Device comparison

Open label device study

Adults aged 18 - 45 & >60 years

Compare PD

Usability

Ongoing

Phase 2a (POSITS)

Is INNA-051 effective in reducing VRI outcomes in community-acquired infections?

1,100 adults
aged 18 - 45
at risk of exposure

IND approved
Aug 2025

Part A Completed May, 2026

Reviewed in Mercuri, Francesca A et al. "Discovery and development of INNA-051, a TLR2/6 agonist for the prevention of complications resulting from viral respiratory infections." Antiviral research vol. 234 (2025)

Candidate drug is Well-Tolerated in Humans

194 Adults exposed thus far

Phase 1* - HVT01, HVT-02 & HVT03

Study Population & Design

Liquid & Dry Powder Formulations

194 participants aged 19+ (up to 81 years old) treated with INNA-051

Up to 900mcg dose assessed as weekly administration on 3 occasions

Safety Summary

No severe or serious TEAEs in the INNA-051 treatment groups

TEAEs were predominantly mild, limited to the nasopharynx, and resolved mostly within 48 hours

No clinically significant changes in clinical chemistry and hematology laboratories

No evidence of systemic pro-inflammatory cytokine release or systemic Type-I interferon release

All PK results below the limit of quantification, confirming minimal systemic bioavailability of drug formulated as a liquid or dry powder

Phase 2a Influenza-Challenge Study*

Study Population & Design

Liquid formulation

82 participants aged 19–53 years treated with INNA-051

3 Arm Study: placebo, 150 and 300 mcg dose

2 doses administered 3 days apart, 1 day before viral challenge

Safety Summary

Mirrored what was observed during Phase 1

Innate activation followed by Large virus inoculum 1 day post treatment did not result in:

- any unexpected or serious treatment-related adverse events
- any enhancement of viral replication

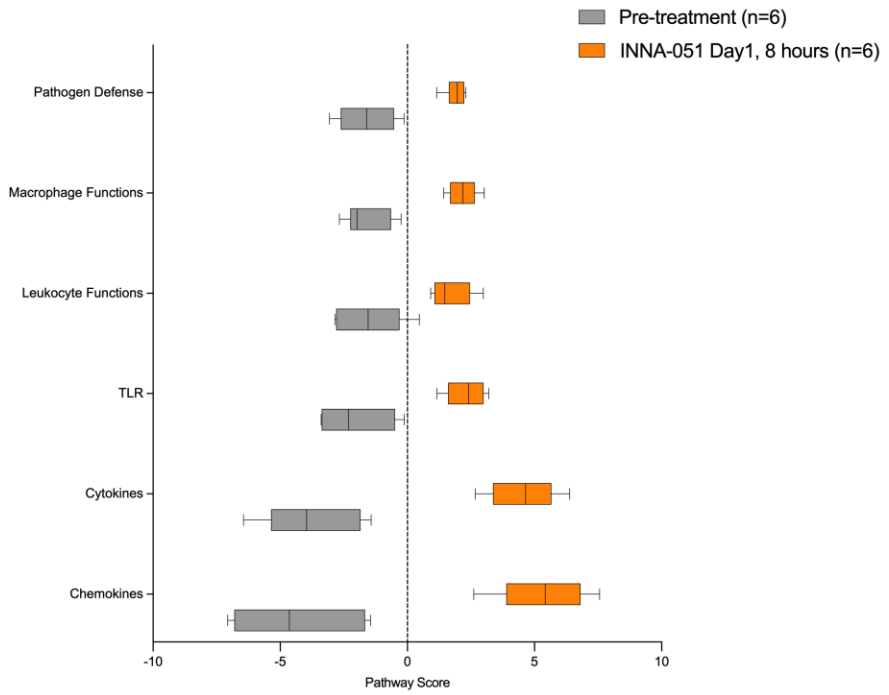
* Mercuri et al. ERJ Open Res (2024); doi.org/10.1183/23120541.00199-2024

Candidate Stimulates Nasal Host Defense Pathways in Humans

Phase 1b study – Dry Powder Formulation in Individuals aged 18 – 45

Differential Gene Expression Analysis of Nasal Samples from Phase 1b Participants

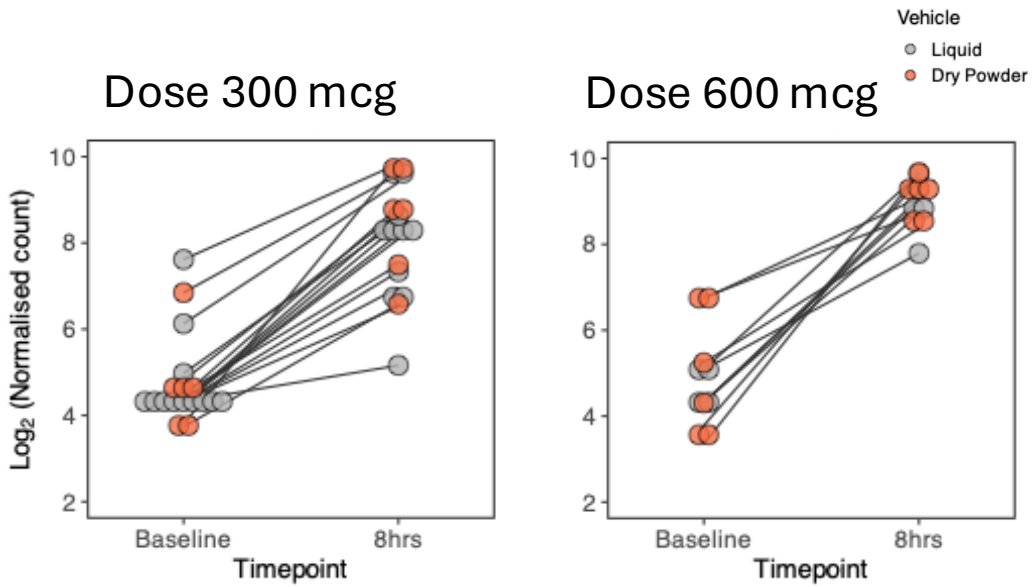
SAD Cohort – 600 mcg dose



Gene expression analysis was performed using the Nanostring Counter Human Pan Cancer Immune Profiling panel from nasal. Pathway scores (x-axis) were calculated using the Nanostring Pathway Module

Dry and Liquid Formulations Show Similar Biological Activities

TLR2 Gene Expression following Treatment
Dry Powder vs Solution Formulations in Adults (18- 50)



n=18 (Liquid n=12/Dry Powder n=6)

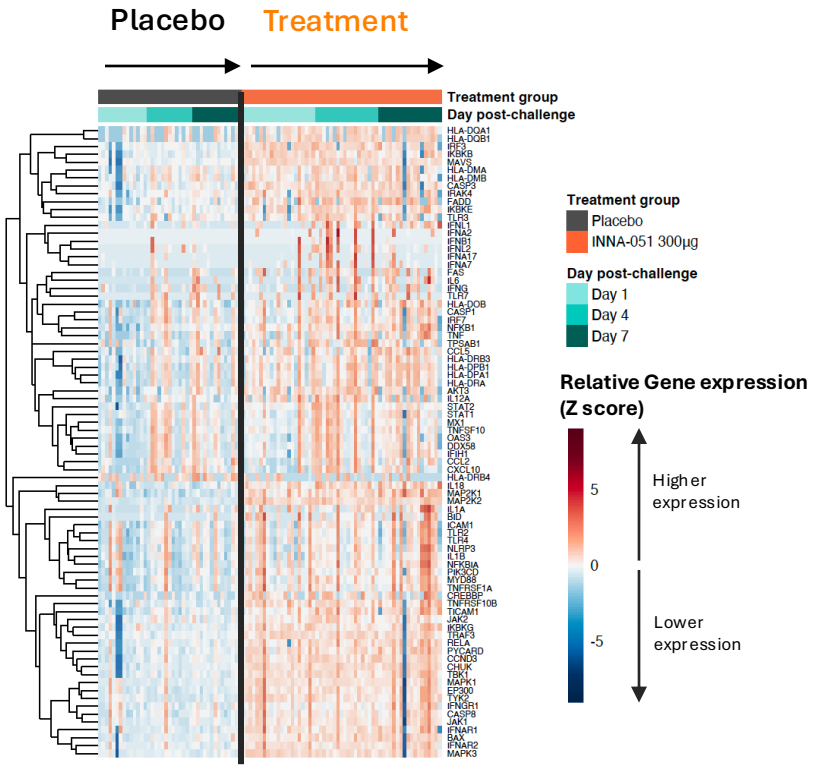
n=10 (Liquid n=4/Dry Powder n=6)

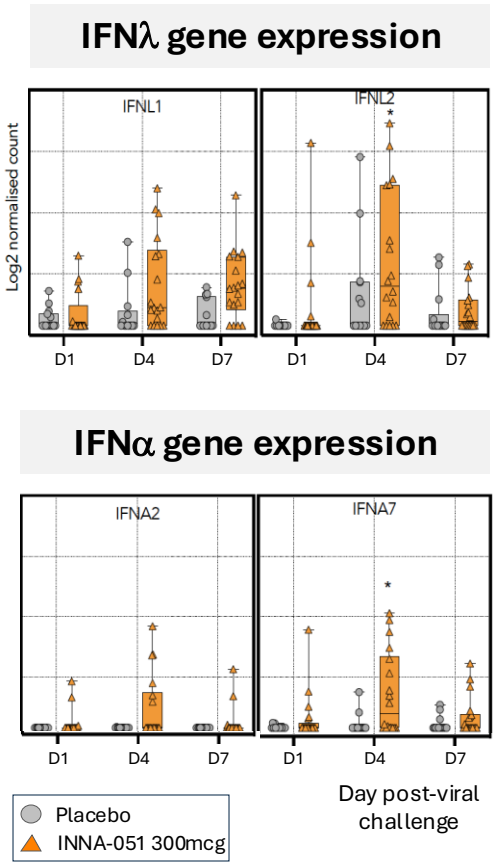
Log2 normalised mRNA counts of TLR2 expression pre-dose and 8h post-dose. Lines connect individual participants.

Candidate Accelerates Viral Clearance in Infected Participants

Phase 2a Influenza-Challenge Study – conducted with a high IAV inoculum: >300,000 $TCID_{50}$

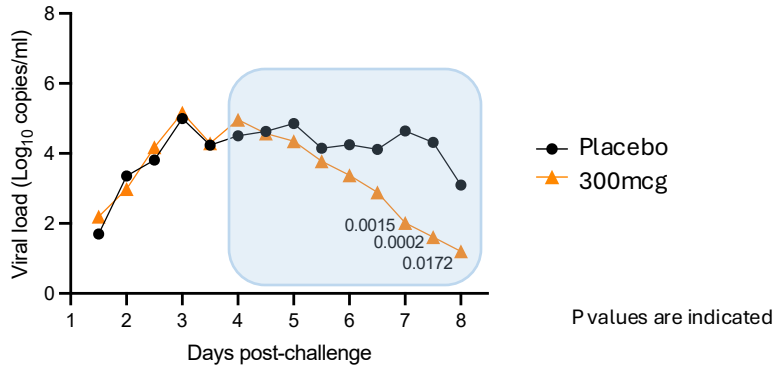
Boosts Influenza Host and Interferon Responses in PCR-confirmed Infected Participants [1]



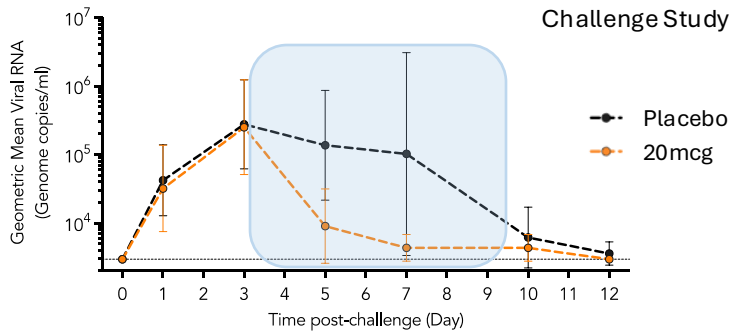


Influenza host response KEGG pathway and IFN gene analysis performed using the Nanostring Counter Human Immune Profiling panel from nasal samples taken from PCR confirmed Infected Participants

Correlates with Accelerated Viral Clearance in PCR-confirmed Infected Participants [1]



Reflects Pre-Clinical Findings [2]



1: Mercuri et al. ERJ Open Res (in press 2024); 2. Proud et al. EBioMedicine (2021)

POSITS Phase 2 POC Seasonal Prophylaxis

Objectives and Design (NCT07222670; 2025-2027)

1

To demonstrate the **safety** and **tolerability** of **seasonal prophylaxis** use in adults

https://positsclinicalstudy.com/#about-respiratory-infection

2

To demonstrate the **efficacy** of candidate in **decreasing the incidence**, **severity** and **duration** of **illness** caused by common respiratory viruses

Incidence of RT-qPCR confirmed symptomatic infection

Respiratory and systemic symptom scores (RiiQ) and ADL (EQ-5D-5L)

Time to symptom resolution

Duration of infection
[Overall and by pathogen]

Exploratory: HCRU, asymptomatic infection

3

Population & Design

Adults 18 - 45 at risk of exposure

Study design (5 sites)

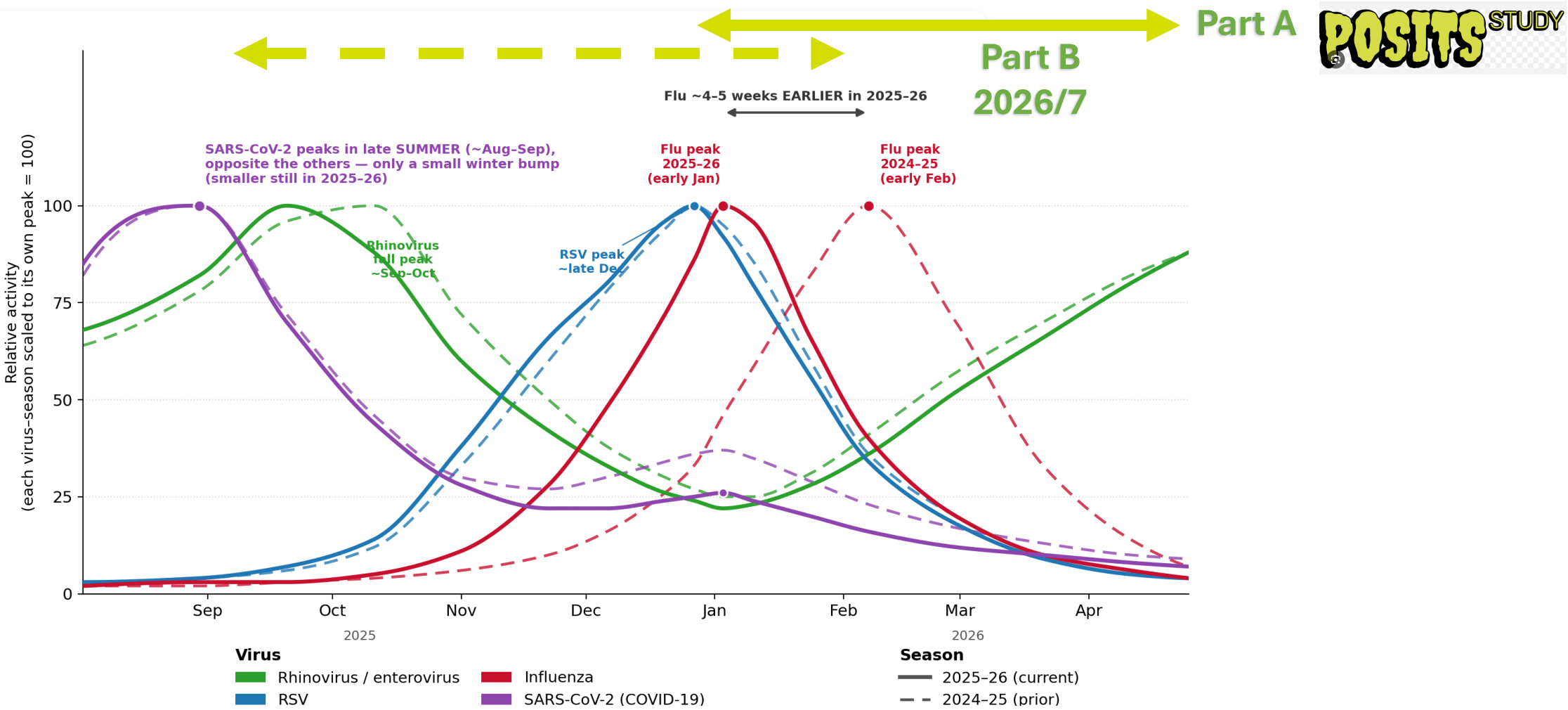
Part A: 4 weekly doses
Part B: 3-month weekly dosing

Part A: 200 1 randomized participants (1:1 ratio)
Part B: 900 randomized participants (1:1 ratio)

- 800: residents in university housing, childcare center workers, and/or those living with a child aged 10 or less attending school or day care
- 200: military personnel

Overlapping respiratory virus peaks — Maryland, 2024–25 vs 2025–26

Relative timing of influenza, RSV, rhinovirus and SARS-CoV-2 across the season (August → April)



Sources: Maryland Combined Respiratory Illness Dashboard & Influenza Dashboard (health.maryland.gov); CDC NREVSS rhinovirus/enterovirus & SARS-CoV-2 regional surveillance (HHS Region 3, incl. Maryland). Illustrative relative-activity curves anchored to reported onset / peak / decline timing — exact weekly counts are not machine-extractable from the state's interactive dashboards, and Maryland does not report rhinovirus separately. Each curve is scaled to its own seasonal peak to compare timing; heights are not comparable between viruses or to case counts.

Summary

The Military`s Role in Advancing this Candidate Drug development

- Since 2022, **funding** from the Capability Program Executive for Chemical, Biological, Radiological and Nuclear Defense (CPE CBRND) in collaboration with the Defense Innovation Unit **supported the development program**:
  - Formulation optimization
  - Manufacturing readiness
  - Nonclinical studies
  - Progression into early-phase clinical evaluation and transition toward a dry powder intranasal formulation

- The ongoing **Phase II study includes military participants** recruited at the NMRC CTC

Conclusion

- The candidate drug is positioned as a prophylactic agent with potential activity against multiple respiratory viruses, reflecting a broader strategy focused on platform-based preparedness rather than pathogen-specific interventions.

- The emphasis on intranasal delivery, stability, and scalability aligns with operational requirements for deployable countermeasures in high-risk or resource-constrained settings.

This case illustrates the role of targeted public-sector funding in advancing early-stage programs with potential relevance to pandemic preparedness, while highlighting the importance of continued evaluation in later-phase clinical studies

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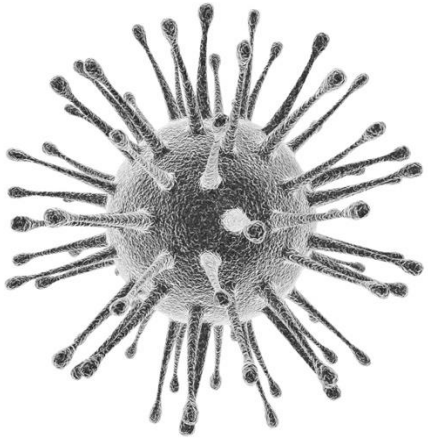

- Material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s), and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of War

- **The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.**

- **Source of support:** This work was supported by ENA Respiratory Investors and CPE CBRND JPM CBRN Medical.

- **Human subject research protections:** The POSITS study NCT07222670 protocol was approved by Advarra with concurrence from the Naval Medical Research Command Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects.

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