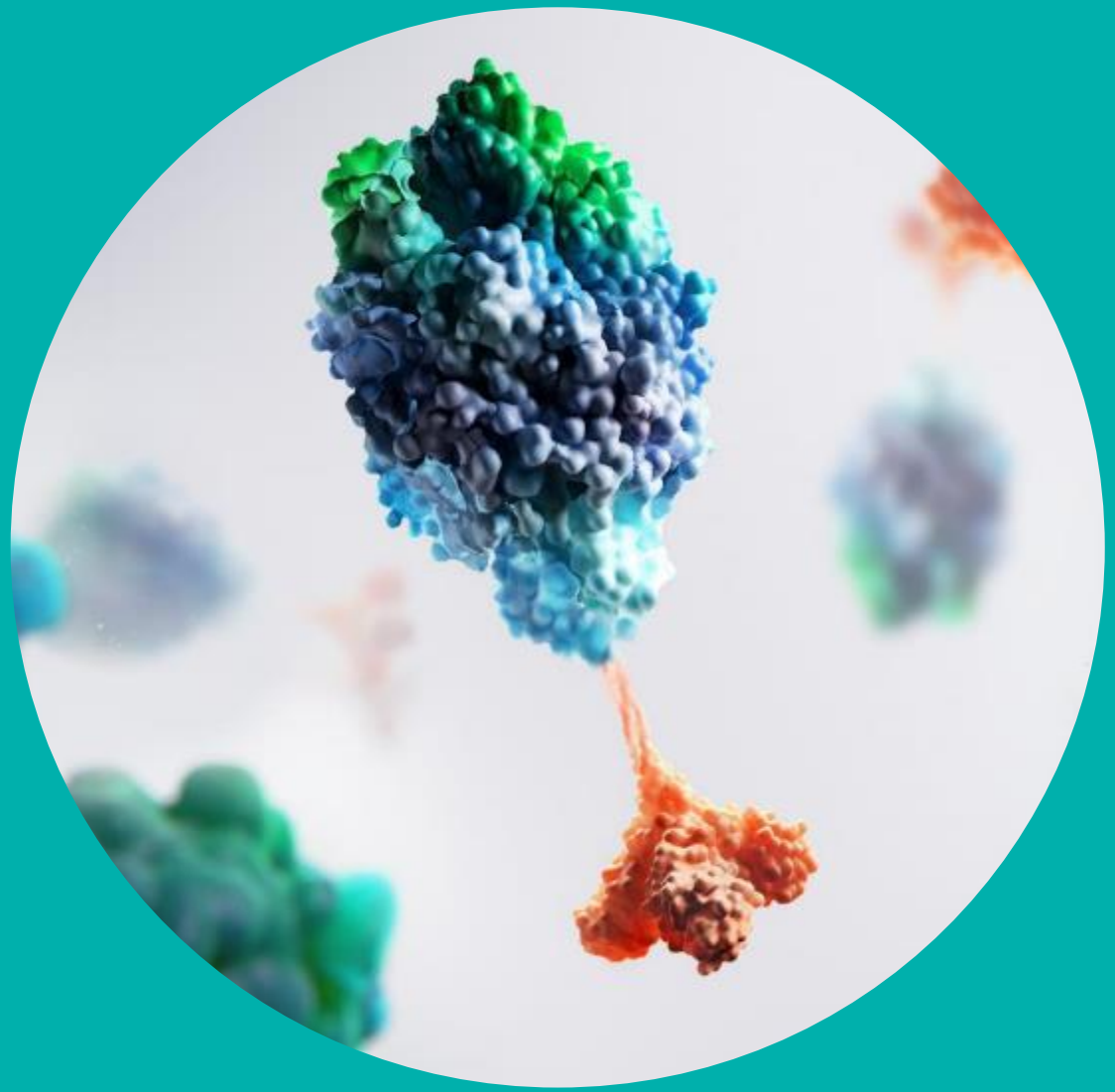


Clover Biopharmaceuticals:
Corporate Overview

January 2026

Disclaimer

This presentation contains certain forward-looking statements and information relating to us and our subsidiaries that are based on the beliefs of our management as well as assumptions made by and information currently available to our management. When used, the words "aim," "anticipate," "believe," "could," "estimate," "expect," "going forward," "intend," "may," "might," "ought to," "plan," "potential," "predict," "project," "seek," "should," "will," "would" and the negative of these words and other similar expressions, as they relate to us or our management, are intended to identify forward-looking statements.

Forward-looking statements are based on our current expectations and assumptions regarding our business, the economy and other future conditions. We give no assurance that these expectations and assumptions will prove to have been correct. Because forward-looking statements relate to the future, they are participant to inherent uncertainties, risks and changes in circumstances that are difficult to predict. Our results may differ materially from those contemplated by the forward-looking statements. They are neither statements of historical fact nor guarantees or assurances of future performance. We caution you therefore against placing undue reliance on any of these forward-looking statements. Any forward-looking statement made by us in this document speaks only as of the date on which it is made. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. Participant to the requirements of applicable laws, rules and regulations, we undertake no obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise. All forward-looking statements contained in this document are qualified by reference to this cautionary statement.

Executive Summary

Clover is Developing Potential Global First-in-Class and Best-in-Class RSV + hMPV ± PIV3 Combination Vaccines (Phase 2 Ongoing) with the Potential Ability to Re-Vaccinate Individuals Previously Receiving Approved RSV Vaccines to Restore and Broaden Protection

Recent Milestones & Catalysts:

- ☑ **July 2025:** $1.6 Billion Acquisition of Vicebio by Sanofi Based on Phase 1 Data for RSV+hMPV Further Validates Global Unmet Need
- ☑ **Oct 2025:** Clover Positive Phase 1 Data for RSV+hMPV±PIV3 Combination Vaccine Candidates and for RSV Revaccination
- ☑ **Jan 2026:** Clover Phase 2 Initiation for RSV+hMPV±PIV3 Combination Vaccine Candidates

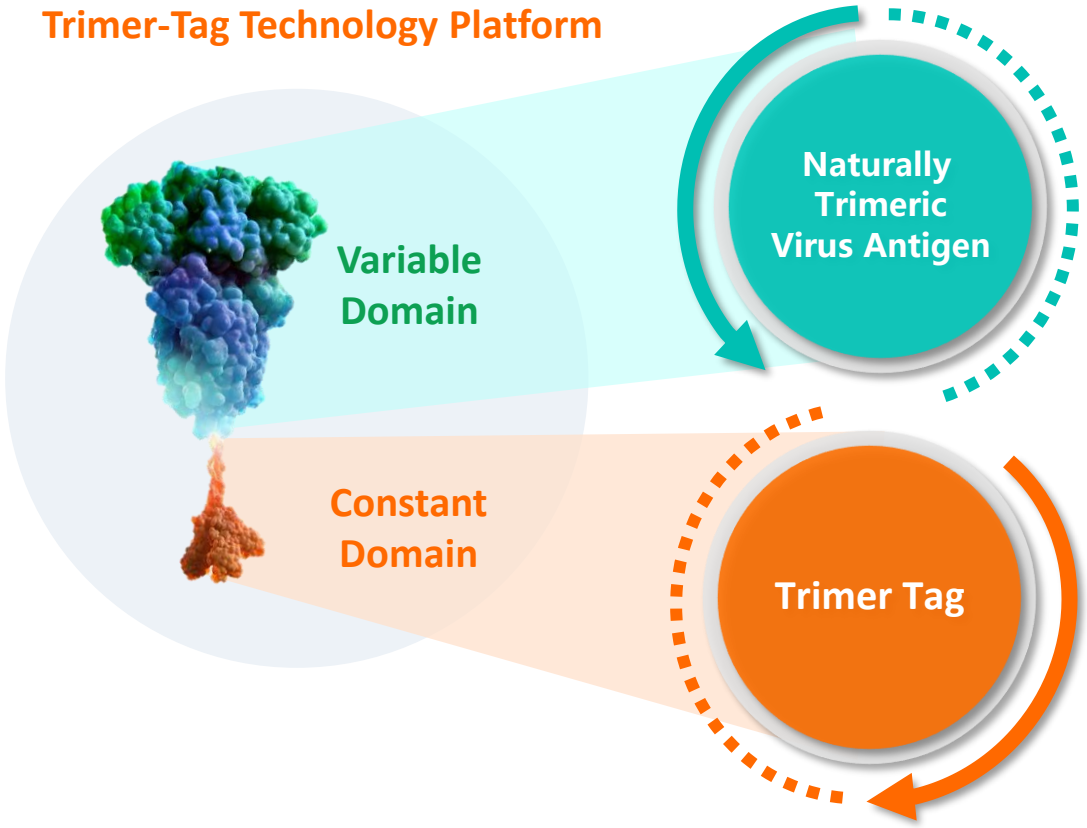
Next Steps:

- ❑ **Ongoing:** Clover to Advance Evaluation of Global Collaboration Opportunities (for Maximum Value Creation)
- ❑ **H1-2026:** Additional Data from Ongoing Phase 1 Trial for RSV Re-Vaccination
- ❑ **2026:** Phase 2 Results for RSV+hMPV±PIV3 Combination Vaccine Candidates

Clover's Trimer-Tag Technology Platform for Vaccine Development

- **Highly Differentiated Vaccine Technology Platform:** The only technology platform globally for producing recombinant covalently-trimerized antigens utilizing a human-derived trimerization tag; the use of covalent bond enables stable naturally-trimeric configuration (induces strong & "native" neutralizing responses); does not induce ADA/pre-existing immunity issue (potentially enables re-vaccination & positive safety profile)
- **Validated Technology:** Platform has been fully validated by COVID-19 vaccine (SCB-2019) that is authorized for Emergency Use in China

Trimer-Tag Technology Platform



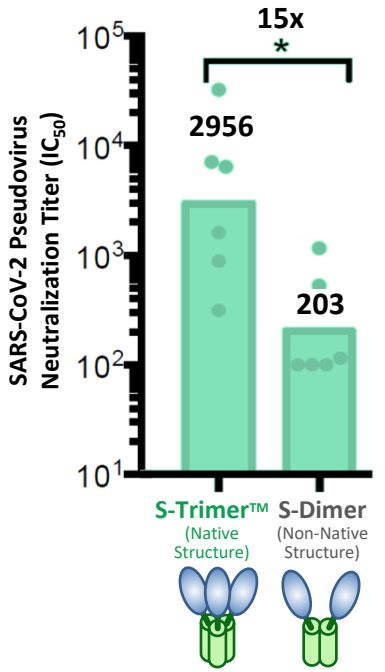
20+ Potential Virus Antigens

Coronavirus | RSV | hMPV | PIV3 | Influenza | EBV | HSV | Rabies | HIV

- ✓ **Trimerizes* any protein of interest**
- ✓ **Achieves stable** covalently-linked and **native-like trimeric structures** of virus antigens
- ✓ **Human-derived**, contributing to favorable safety profile and no ADA observed in Phase 2/3 for SCB-2019 (CpG 1018/Alum)
- ✓ **Secreted** trimeric fusion proteins produced in mammalian cells; **affinity-purification** achieves high antigen purity

Strong Neutralizing Immune Responses

Trimer-Tagged Native-Like Spike Antigens Induce Superior Immune Responses Compared to Non-Native Conformations (e.g., Dimeric Spike) (1)

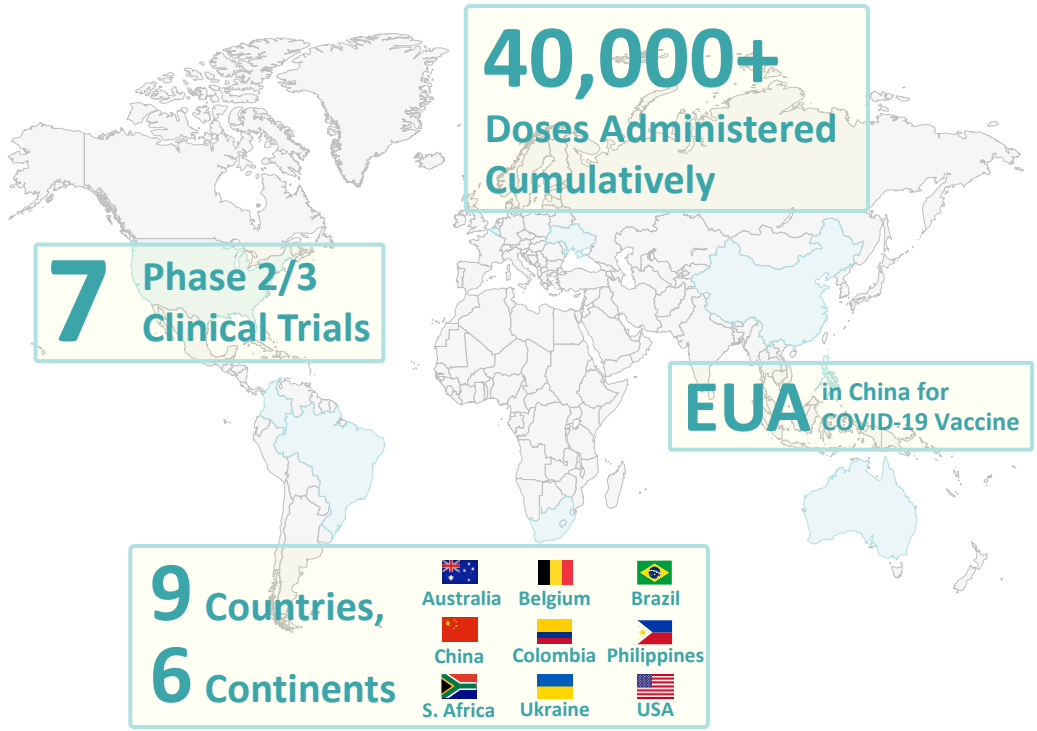


Note: Representative list of viruses with naturally trimeric spike antigens is illustrative and not exhaustive. Abbreviation: ADA (Anti-Drug Antibodies).
* A "trimer" refers to a molecule or an anion formed by combination or association of three molecules or ions of the same substance. Trimerization is a chemical reaction that uses three identical molecules to produce a single trimer. Proteins that are created through the joining of two or more genes that originally coded for separate proteins and consist of three identical simpler parts are referred to as "trimeric fusion proteins". Trimerization tag refers to a protein tag from the C-propeptide domain of procollagen (Trimer-Tag), which is capable of self-assembly into a disulfide bond-linked trimer.
(1) SARS-CoV-2 pseudovirus neutralizing antibody responses in mice vaccinated with two doses of S-Trimer (Trimer-Tagged SARS-CoV-2 spike protein) or S-Dimer (Fc-Tagged SARS-CoV-2 spike protein) on Days 0 and 21. Data based on sera collected on Day 35 (14 days after second dose).

Trimer-Tag: *A Safe, Potent & Validated Vaccine Platform*

Extensive Clinical Experience Globally

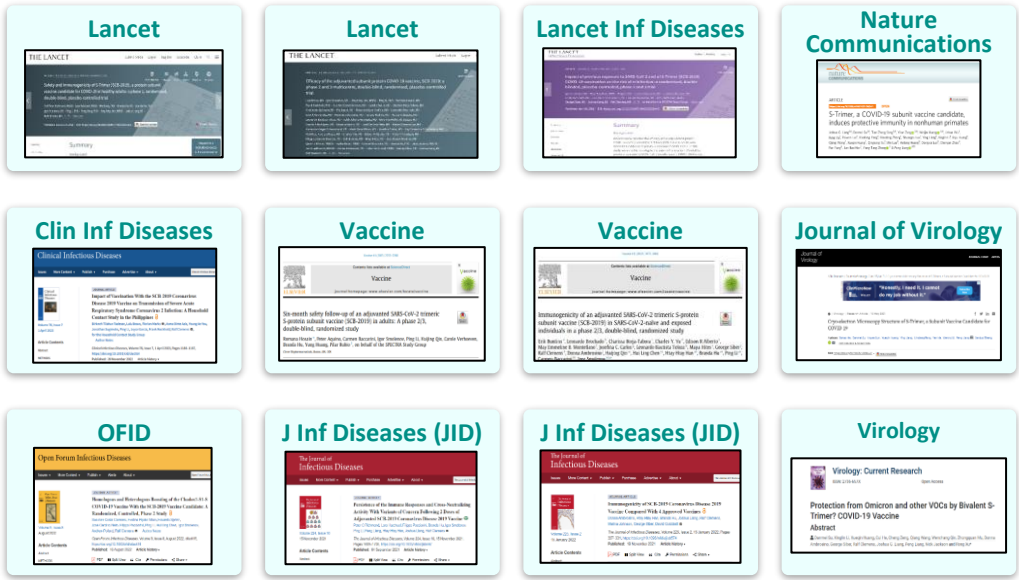
- ☑ **40,000+ Doses Administered Across 9 Countries & 6 Continents**
- ☑ **Experience in Broad Population Groups** (Elderly, Adult, Adolescent, Co-Morbidities (1)), **Races & Ethnicities**



(1) Subjects enrolled with co-morbidities (associated with high risk of severe COVID-19) include chronic kidney disease, chronic obstructive pulmonary disease, obesity with BMI ≥30 kg/m2, serious heart conditions such as hypertension, heart failure, coronary artery disease or cardiomyopathies, and Type 2 diabetes mellitus.

Endorsed by Leading Scientific Community

- ☑ **Received US$ 397 Million Funding from CEPI to Support Clover Establishing its Vaccine Platform** (Trimer-Tag Platform + Vaccine Manufacturing Capabilities)



- ☑ **Trimer-Tag Platform Published in the Most Renowned Scientific Journals Globally** (Lancet, Nature Communications, JID, etc.)

CLOVER BIOPHARMACEUTICALS

RSV is a Validated Blockbuster Market; Expansion is Dependent on Addressing 2 Unmet Needs

☑ RSV Vaccines Have Generated ~US$ 4 Billion Product Sales in First 2 Years of Launch (2023-2024)

~15 Million Doses Administered to Older Adults in U.S. (1)

Fastest Vaccine in History to Achieve Blockbuster Status (2)

- AREXVY (GSK) and ABRYSVO (Pfizer) Launched in the U.S. in AUG-2023
- ~US$ 2.5 Billion Sales Generated in H2-2023

However, Sales Fell by ~37% in 2nd Year of Launch (2024)

- ~US$ 1.5 Billion Sales Generated in 2024
- **Key Problem 1: Initial Dose** Uptake in Older Adults Plateaued at ~40% (1)
- **Key Problem 2: Re-Vaccination** is Not Supported Based on Lackluster Clinical Data, Despite Waning Efficacy ~2 Years After Initial Dose (3)
- Continued Decline in U.S. Sales is Expected in 2025

(1) U.S. CDC Weekly RSV Vaccination Dashboard (data as of Q2-2025). Adults ≥60 years of age.
(2) Excluding pandemic vaccines.
(3) GSK ACIP Presentation (26-JUNE-2024) and press release (08-OCT-2024).
(4) Retail Pharmacy Cost.

2 Key Unmet Needs & Opportunities to Unlock RSV Market Expansion:

RSV Combination Vaccines (RSV + hMPV ± PIV3)

Opportunity to Increase Uptake & Optimize Pricing, by Significantly Increasing Breadth of Protection

- ~40% Uptake of RSV Vaccines in Older Adults(1) is Still Significantly Lower than Seasonal Influenza Vaccine Uptake of Up to ~60% (3)
- In the Same Family of Viruses as RSV, Human Metapneumovirus (hMPV) and Parainfluenza Virus Type 3 (PIV3) Drive Significant Lower Respiratory Tract Disease (LRTD) in Older Adults and Infants
- Current U.S. Pricing of ~$300/Dose for Standalone RSV Vaccines (4)

Re-Vaccination

Opportunity to Multiply Market Value if Effective Re-Vaccination Can be Demonstrated

- Efficacy of Protein-Based RSV Vaccines (AREXVY and ABRYSVO) Wanes After ~2-3 Years (3)
- ~15 Million Older Adults (≥60 Years) in U.S. Previously Receiving RSV Vaccines would Benefit Significantly from Effective Re-Vaccination
- Routine Re-Vaccination Every 2-3 Years is Potentially Needed to Restore Peak Levels of Protection

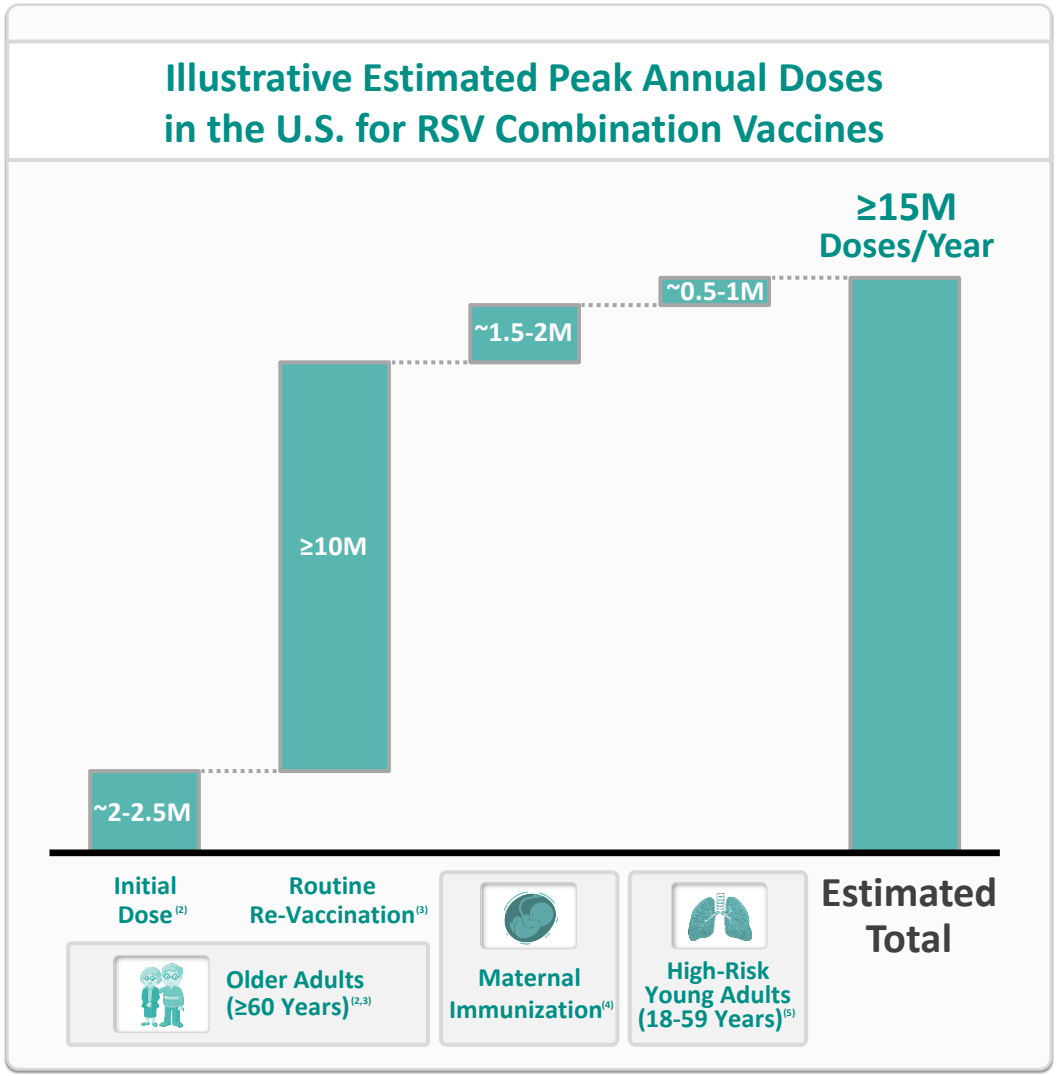
$10 Billion+ Potential Peak Sales Globally for RSV Combo Vaccines with Ability to Re-Vaccinate

$10 Billion+ Potential Global Peak Sales for RSV Combination Vaccines with the Ability to Re-Vaccinate [1]

- Precedent: ~$8 Billion Global Sales in 2024 for Respiratory Pneumococcal Vaccines (Prevnar, PPSV, etc.)

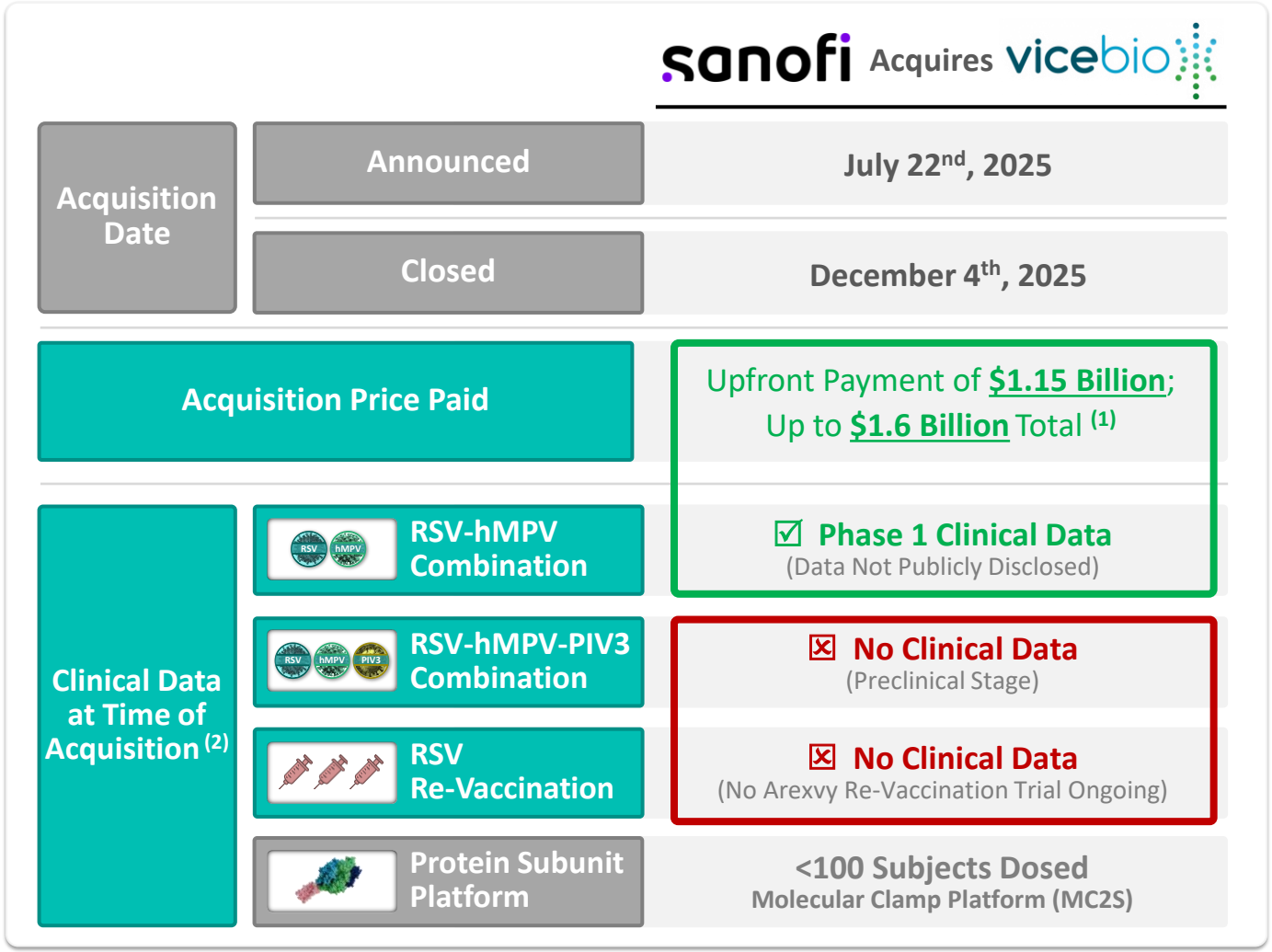
$7 Billion+ (15 Million+ Doses/Year) Opportunity in U.S.

- ~$2.5 Billion Sales for Standalone RSV Vaccines (Arexvy/Abrysvo) in First ~5-Months of Commercial Launch in H2-2023 De-Risks Commercial Launch of Future RSV Combination Vaccines
- Existing Pool of ~15 Million Older Adults in the U.S. Previously Vaccinated Standalone RSV Vaccines Provides Bolus Opportunity for Rapid Uptake for Re-Vaccination with RSV Combination Vaccines



Note: Preliminary and illustrative for discussion purposes only. Subject to change based on emerging data and assessments. Pneumococcal vaccine annual sales from company reports.
[1] Assumes net pricing for RSV combination vaccines of $400-500 per dose; assumes 2:1 geographical sales ratio between U.S. and ex-U.S. sales based on Prevar sales in 2023-2024 (company reports); U.S. total population assumptions based on Statista (2023); **[2]** Assumes 3.5-4.0 million total new older adults per year and up to 60% uptake of RSV combination vaccines; **[3]** Assumes re-vaccination interval of 2-3 years, average remaining lifespan of 25 years for older adults reaching 60 years of age and approximately 60% compliance rate for re-vaccination, resulting in approximately 5 re-vaccination doses after the initial dose in a given older adult individual; **[4]** Assumes approximately 3.5 million total pregnant women annually (U.S. CDC National Center for Health Statistics, 2024) and approximately 40-50% uptake based on ~39% uptake of Abrysvo maternal immunization as of H1-2025 (ACIP Meeting Presentations 25-JUNE-2025); **[5]** Assumes 20-25 million total adults aged 18-59 years, and approximately 9.5% and 24% of U.S. adults 18-49 years and 50-64 years of age, respectively, having increased risk of hospitalization from RSV-LRTD including those with underlying chronic conditions such as obesity, diabetes, COPD, heart failure, chronic kidney disease and asthma (U.S. CDC "Morbidity and Mortality Weekly Report" 15-AUG-2024), and uptake of approximately 40-50% for receiving one dose of RSV combination vaccine (re-vaccination would represent further upside).

Sanofi Acquires ViceBio for Up to $1.6 Billion Based on RSV-hMPV Combo Phase 1 Data



Sources: Public Announcements & Company Websites. As of January 2026.
Note: For illustrative discussion purposes-only.
(1) Up to US$ 450 million in development & regulatory milestone payments.
(2) NCT06556147.

Blockbuster Acquisition Based on ViceBio's Phase 1 RSV-hMPV Combination Clinical Data Further Validates Significant Global Unmet Need and Large Pharma BD Interest in the Field

Clover is Currently the Only Other Company with a Clinical-Stage RSV-hMPV Combo Vaccine

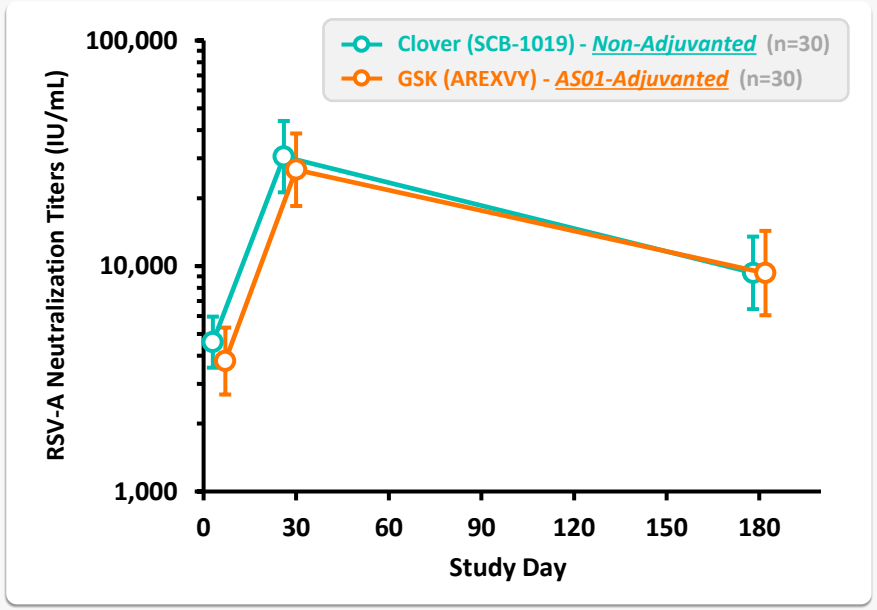
- Clover also has the First Ever and Only Clinical-Stage Protein-Based RSV-hMPV-PIV3 Combination Vaccine
- Clover is also Running the First Ever Heterologous RSV Re-Vaccination Clinical Trial

Prior Phase 1 Clinical Validation of Clover's RSV PreF (SCB-1019) Versus GSK (AREXVY) – *Oct 2024*

Australia Phase 1

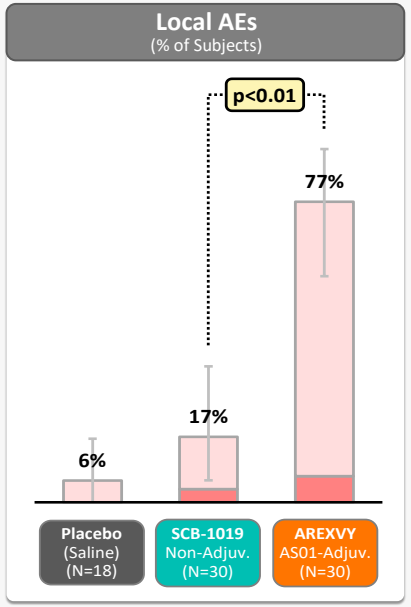
Demonstrated Best-in-Class Combined Immunogenicity & Tolerability Profile as an Initial Dose in RSV Vaccine-Naïve Older Adults, for Non-Adjuvanted SCB-1019 (Clover RSV PreF) Head-to-Head Versus AS01-Adjuvanted AREXVY (GSK RSV PreF)

RSV Neutralizing Antibody Titers (IU/mL)



☑ **Comparable RSV Neutralizing Antibodies at 1-Month** (GMFR ~6-7x) **and Durability Through 6-Months** (GMFR ~3x)

Safety & Reactogenicity



Safety & Reactogenicity Results

- ☑ **Significantly Lower Rates of Local AEs Observed for Clover's non-adjuvanted SCB-1019 (16.7%) Versus GSK's AS01-adjuvanted AREXVY (76.7%)**
- ☑ **SCB-1019 Local and Systemic AEs were Generally Mild for SCB-1019 and were Comparable to Saline Placebo**
- ☑ **No Vaccine Related Serious Adverse Events (SAEs), Adverse Events of Special Interest (AESIs), or AEs Leading to Discontinuation Observed**

☑ **Superior Local Tolerability + Clean Safety Profile**
(Additionally: 40,000+ Doses Human Safety Database for Trimer-Tag Platform)

Abbreviations: IU/mL (International Units Per Milliliter), GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise).
Note: Dots represent GMTs (± 95% confidence intervals). RSV-A neutralizing antibodies are shown above; RSV-B neutralizing antibody results are comparable.
RSV neutralization titers expressed as IU/mL calculated using comparison to NIBSC 16/284 reference sera.
Assay conducted at third-party testing laboratory using validated RSV neutralization assays.

Note: Percentage of older adult subjects (60-85 years) experiencing selected adverse events (AEs) following vaccination with RSV vaccine (30 subjects/group) or saline placebo (18 total placebo subjects across entire Phase 1 study). 95% confidence intervals shown. Light pink bars represent mild AEs, and darker pink bars represent moderate AEs. No severe AEs observed.

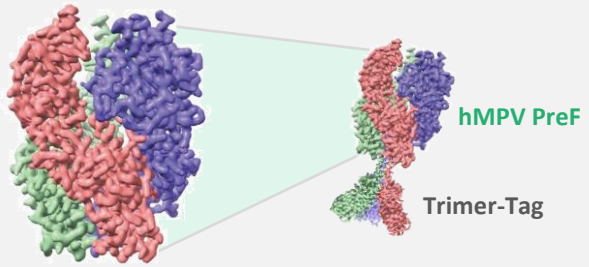
CLOVER BIOPHARMACEUTICALS

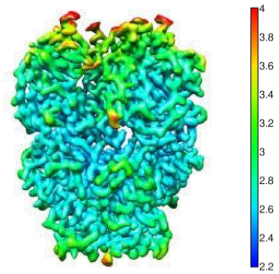
Clover has Achieved Stable PreF-Trimer Conformations for its hMPV and PIV3 Antigens

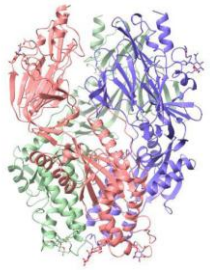
Leveraged RSV PreF & Trimer-Tag Platform Experience to Develop Trimeric hMPV and PIV3 Antigens

Cryo-EM Structures for Clover's hMPV and PIV3 PreF Antigens Resolved (<3Å Resolution)

Clover hMPV PreF-Trimer



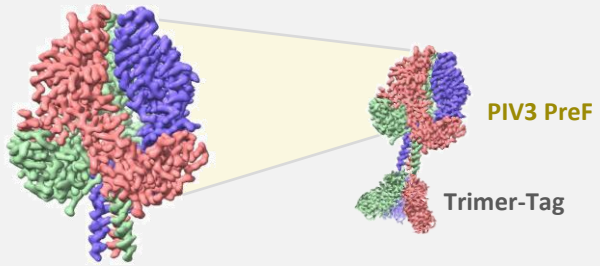


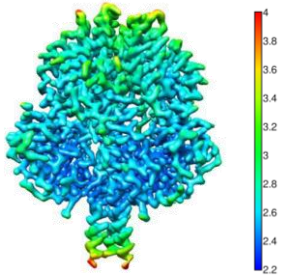


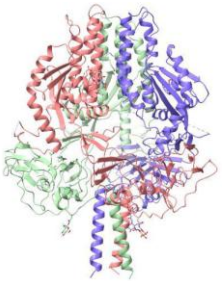
☑ 2.66Å Resolution

PDB Model

Clover PIV3 PreF-Trimer







☑ 2.82Å Resolution

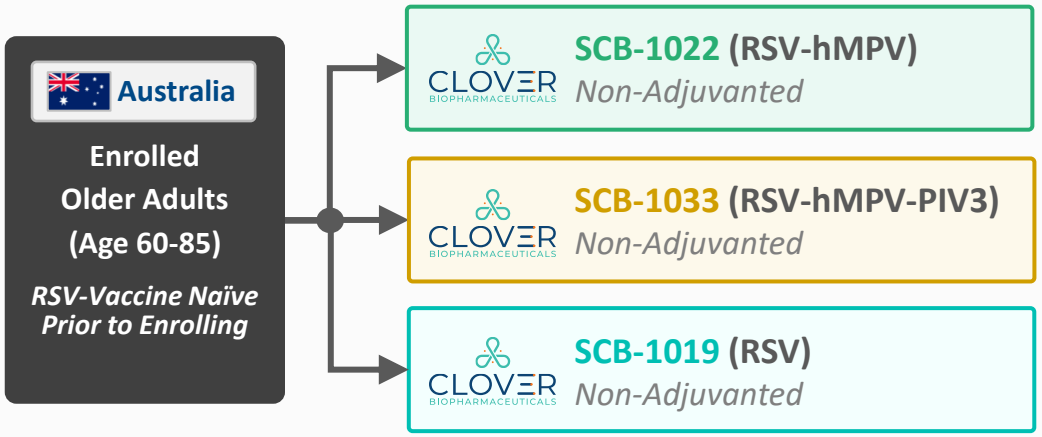
PDB Model

Note: Clover preclinical studies. Cryo Electron Microscopy (EM) results shown.

CLOVER BIOPHARMACEUTICALS

Results Announced from Two Ongoing Phase 1 Clinical Trials (Oct-2025)

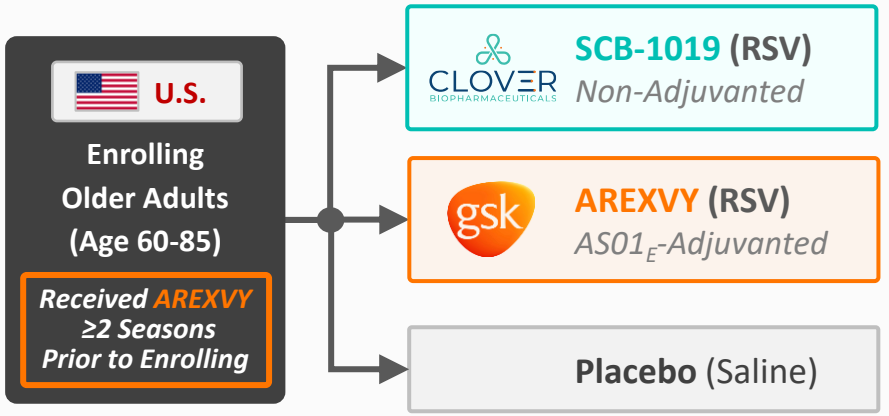
Phase 1: RSV-hMPV-PIV3 Combination Vaccines



Full Immunogenicity & Safety Results in 144 Participants (n=48/Group) for the Selected Dose Levels

NCT06984094.

Phase 1: RSV Re-Vaccination



Interim Analysis Results from 34 Participants for SCB-1019 (n=16), Arexvy (n=15), Placebo (n=3)

NCT06843317.

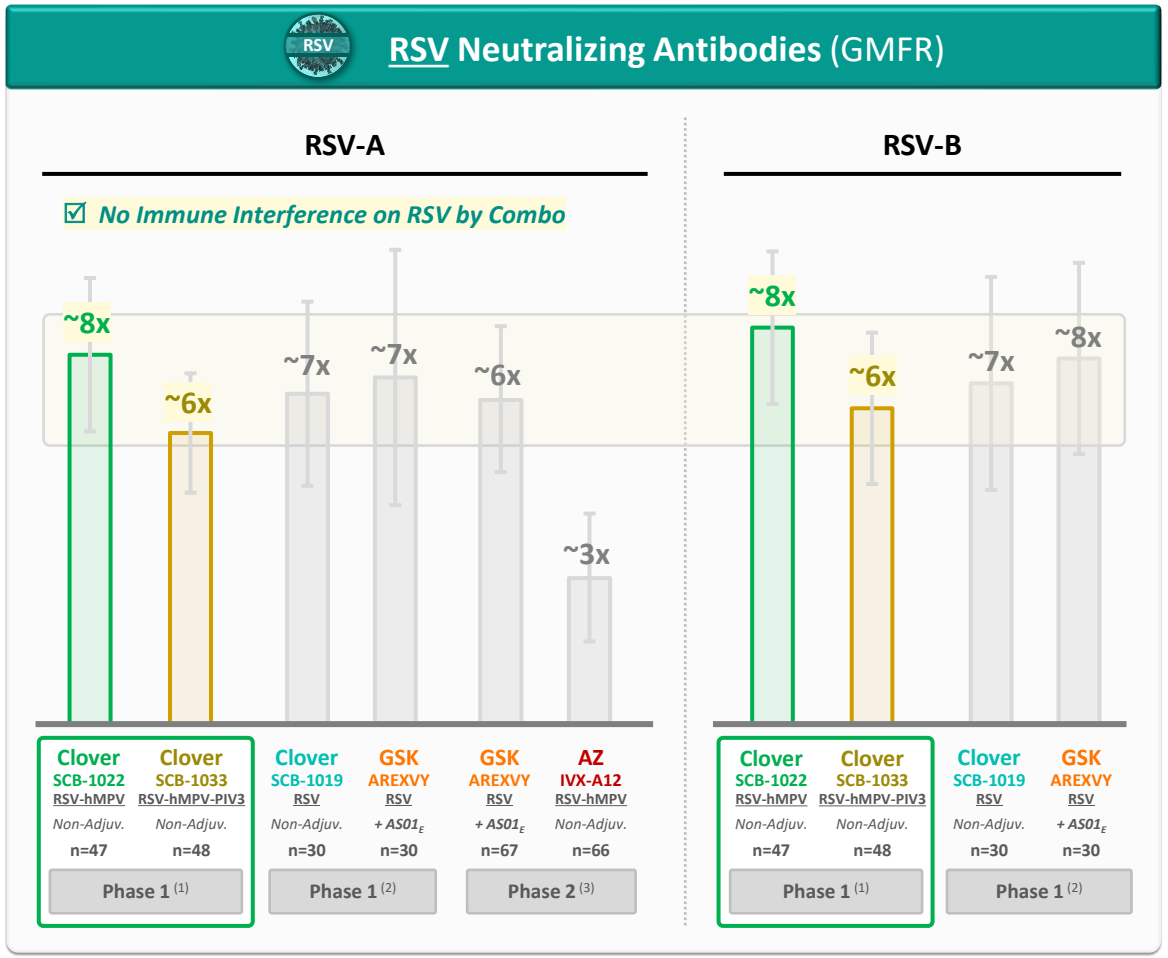
Phase 1 Immunogenicity Results (RSV and hMPV)

Australia Phase 1

Potential Best-In-Class RSV and hMPV Neutralizing Antibody (nAb) Responses for SCB-1022 and SCB-1033, with No Immune Interference on RSV

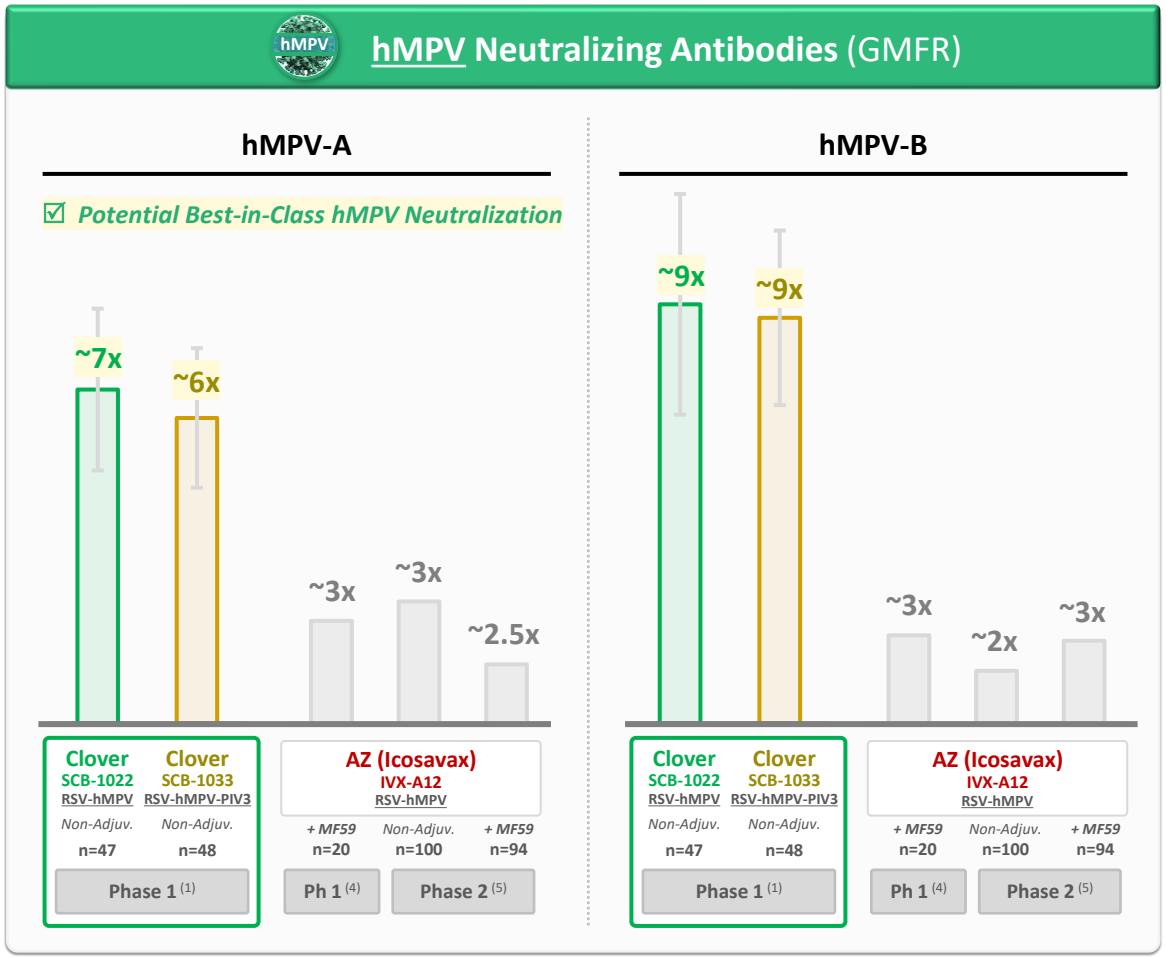
~6-8 Fold Increases in RSV nAbs

RSV Neutralizing Antibodies (GMFR)



~6-9 Fold Increases in hMPV nAbs

hMPV Neutralizing Antibodies (GMFR)



Notes: Clover preliminary results. **Cross trial comparisons for illustrative purposes only.** Geometric mean fold rises (GMFRs) for 1-month post-vaccination versus baseline titers shown for neutralizing antibodies (±95% confidence intervals) in evaluable participants for the selected dose levels.
Sources: **[1]** NCT06984094, **[2]** NCT06194318, **[3]** NCT06481579, **[4]** NCT05664334 (DOI: 10.1093/ofid/ofaf160); **[5]** NCT05903183 (ISIRV RSV Symposium Presentation in MAR-2025).

CLOVER BIOPHARMACEUTICALS

Phase 1 Immunogenicity Results (PIV3)

Australia Phase 1

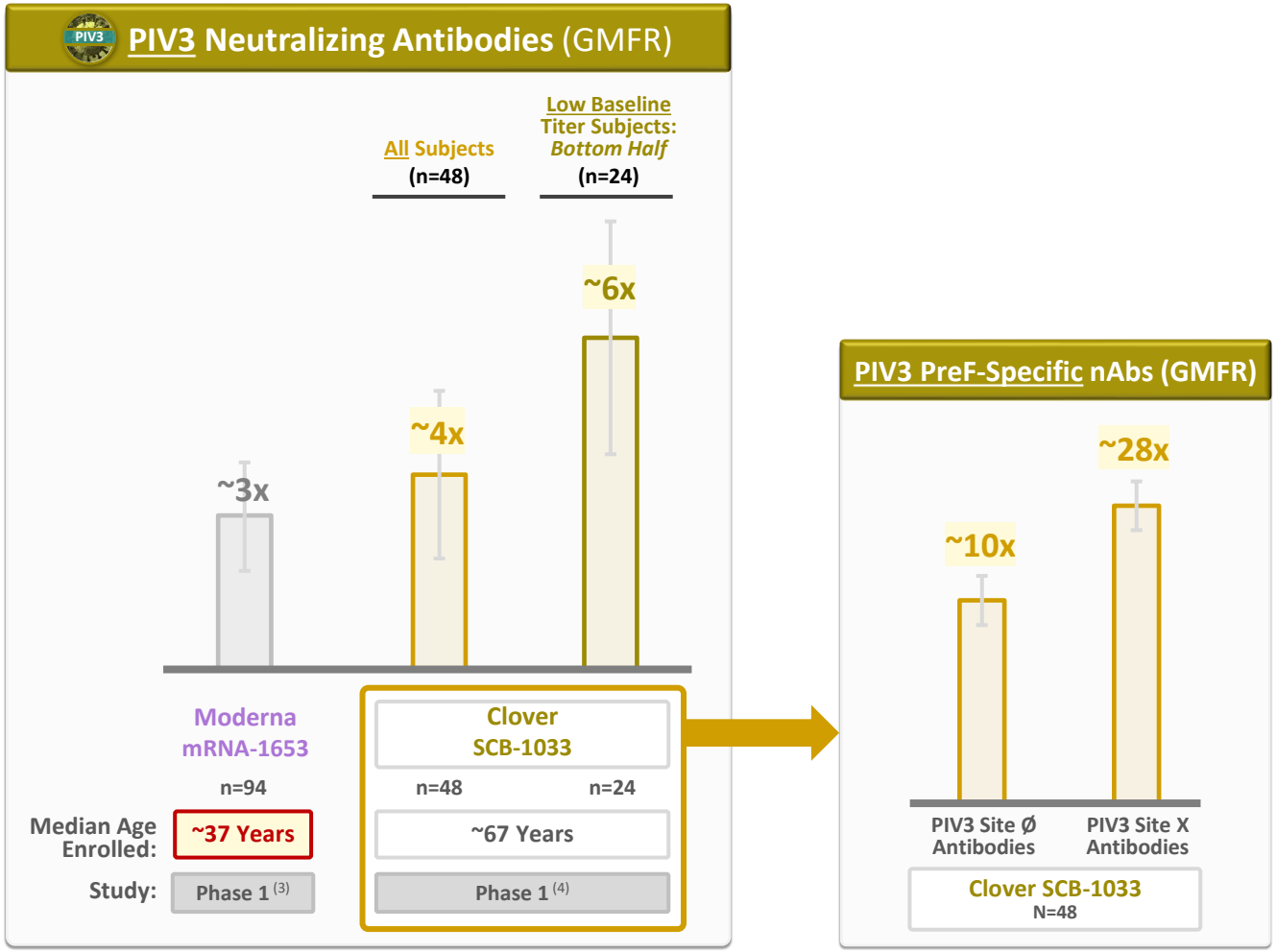
Potential Best-In-Class PIV3 Neutralizing Antibody (nAb) Responses for SCB-1033, Driven by ≥10-Fold Increases in PIV3 PreF-Specific Antibodies

~4-Fold Increases in Total PIV3 nAbs for SCB-1033

- ~6-Fold Increases in Total PIV3 nAbs in participants with low pre-existing baseline PIV3 nAb levels in the bottom 50th percentile (n=24)
- Stronger responses in people who may be most at-risk for infection and disease (with low baseline titers)

Driven by ≥10-Fold Increases in PIV3 PreF-Specific Abs

- PIV3 PreF-specific nAbs (such as Site Ø and Site X) can potently neutralize the PIV3 virus [1]
- However, unlike RSV and hMPV, majority of pre-existing PIV3 nAbs at baseline are against the PIV3 HN protein (whereas levels of pre-existing PIV3 nAbs against the PIV3 PreF protein at baseline are low) [2]
- Therefore, a numerically lower increase in total PIV3 nAbs induced by SCB-1033 (containing PIV3 PreF antigen) – as compared to increases in RSV and hMPV nAbs – is expected



Notes: Clover preliminary results. **Cross trial comparisons for illustrative purposes only.** Geometric mean fold rises (GMFRs) for 1-month post-vaccination versus baseline titers shown for PIV3 neutralizing antibodies and competitive-ELISAs (±95% confidence intervals) for the selected dose level.
Sources: **[1]** DOI: 10.1038/s41467-023-36459-3, **[2]** DOI: 10.1038/s41564-024-01722-w, **[3]** NCT06984094, **[4]** NCT03392389 Moderna mRNA-1653 (hMPV-PIV3 combo) Phase 1 Results (DOI: 10.1093/ofid/ofac206).

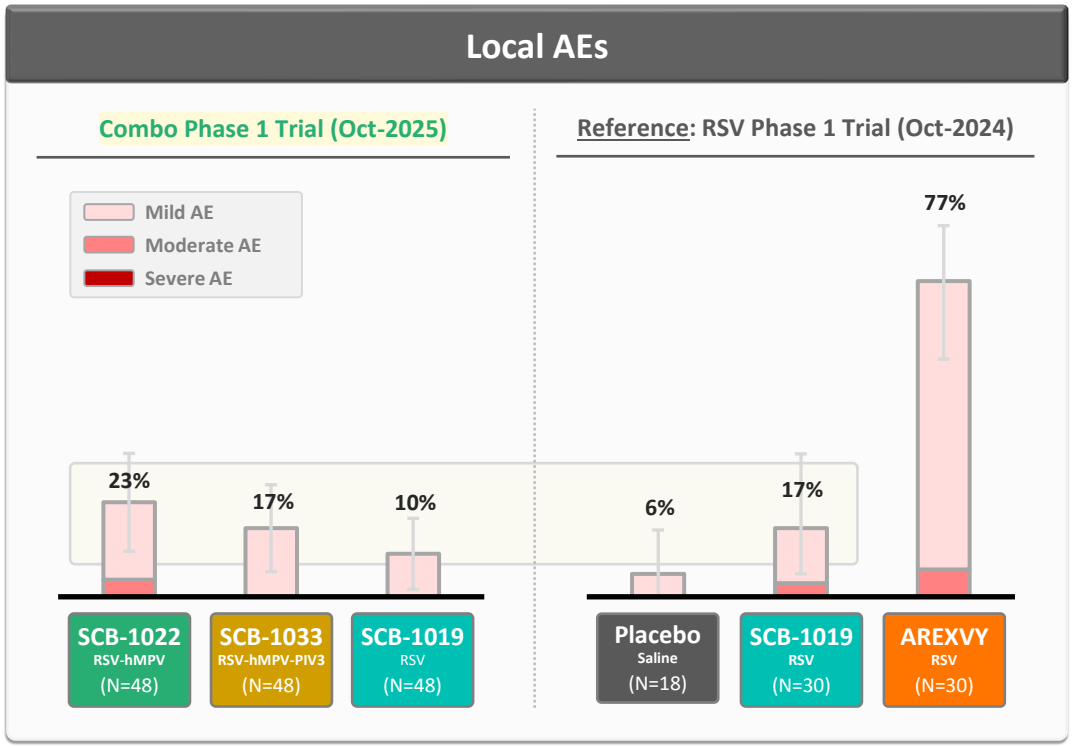
CLOVER BIOPHARMACEUTICALS

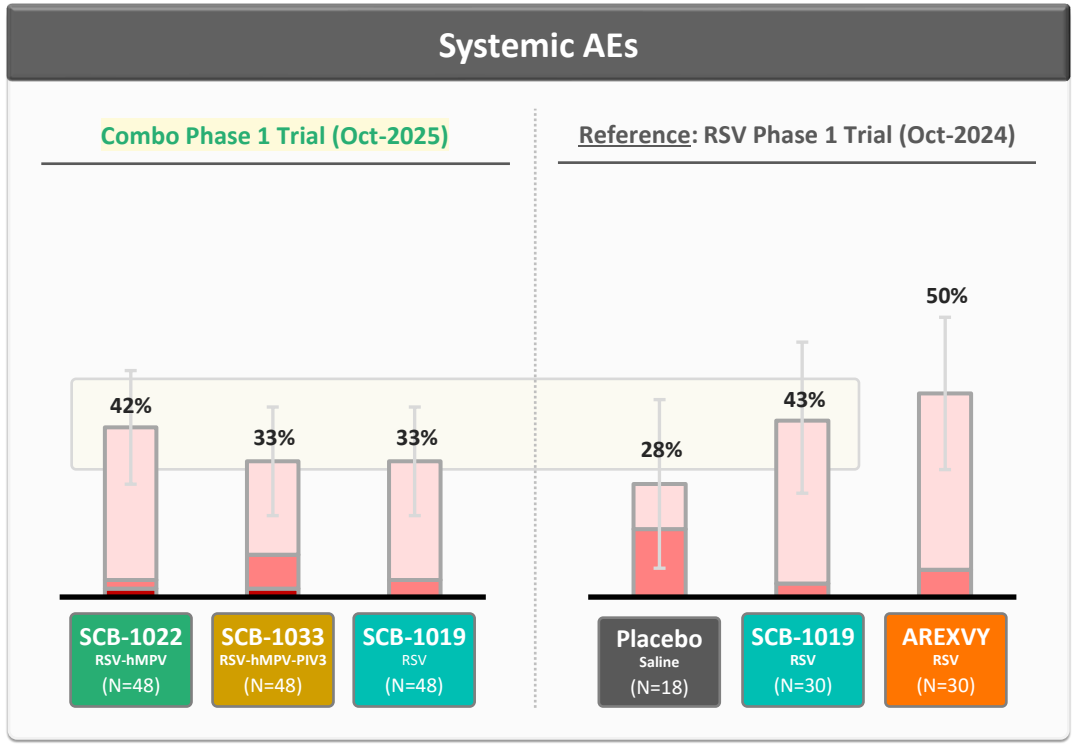
Potential Best-in-Class Safety & Tolerability Profiles for SCB-1022 and SCB-1033

Local and Systemic AEs for SCB-1022 (RSV-hMPV) and SCB-1033 (RSV-hMPV-PIV3) were Generally Mild and Comparable to SCB-1019 (RSV)

- Expected to Compare Favorably Versus **AREXVY (GSK)**, Based on Results from Previous Head-to-Head Clinical Trial

No Serious Adverse Events (SAEs), Adverse Events of Special Interest (AESIs), or AEs Leading to Discontinuation Related to Study Vaccines





Note: Clover preliminary results. **Cross trial comparisons for illustrative purposes only.** Percentage of older adult subjects (60-85 years) experiencing solicited adverse events (AEs) following vaccination are shown (± 95% confidence intervals).

Re-Vaccination Issues Observed for Currently Approved RSV Vaccines, Despite Waning Efficacy of Initial Dose

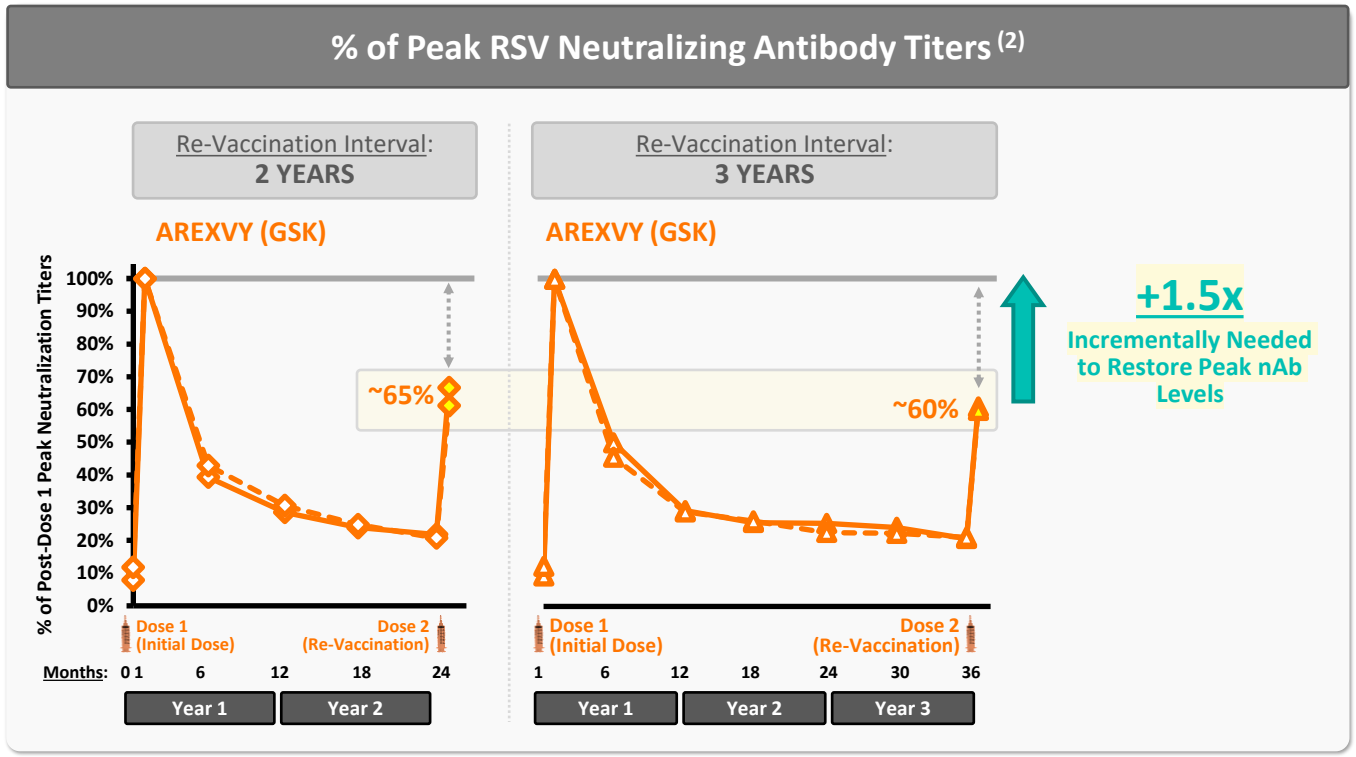
An Incremental ~1.5x Higher nAb Response for Re-Vaccination with SCB-1019 Compared to AREXVY May be Able to Restore Peak Levels of nAbs & Protection

AREXVY Vaccine Efficacy Falls to <50% in ~2 Years After the Initial Dose [1]

- AREXVY vaccine efficacy of ~83% in Year 1, ~56% in Year 2 and ~48% in Year 3 [1]

However, AREXVY Re-Vaccination Boosts RSV nAbs Only Up to ~60-65% of Peak Levels [2]

- AREXVY re-vaccination was not associated with incremental vaccine efficacy [3]
- Similar re-vaccination issues observed for ABRYSVO (Pfizer) [4]
- Both AREXVY and ABRYSVO utilize the same T4-Foldon trimerization motif and similar Cav1 PreF stabilization approaches, whereas Clover utilizes Trimer-Tag and a differentiated PreF stabilization approach



Note: **Cross trial comparisons for illustrative purposes only.** Solid orange lines represent RSV-A nAb titers, and dotted orange lines represent RSV-B nAb titers.

Sources: **(1)** GSK ACIP Presentation (26-JUNE-2024) and press release (08-OCT-2024), **(2)** GSK ACIP Presentation (16-APR-2025), **(3)** GSK ACIP Presentation (21-JUNE-2023),based on primary efficacy endpoint (RSV-LRT ≥2 Symptoms/Signs). **(4)** DOI: 10.1093/infdis/jiae185.

Phase 1 RSV Re-Vaccination Immunogenicity Results (Interim Analysis)

U.S. Phase 1

≥1.6x Higher Trend in RSV nAb Responses Observed for SCB-1019 Compared Head-to-Head Versus AREXVY Re-Vaccination

1.6-1.8x Higher Trend in RSV nAbs for SCB-1019

- ~60% higher trend in GMFRs for RSV-A nAbs versus AREXVY
- ~80% higher trend in GMFRs for RSV-B nAbs versus AREXVY

Driven by Double the % of Participants with Increases (≥2-Fold) in RSV nAbs for SCB-1019

- 69-75% responders for SCB-1019 heterologous re-vaccination
- 33-40% responders for AREXVY homologous re-vaccination

Consistent Randomization & Baseline Profiles

- Baseline characteristics (baseline RSV nAb titers, participant age, re-vaccination interval) in the SCB-1019 and AREXVY groups were highly comparable
- Baseline RSV nAb titers prior to re-vaccination in this study were approximately 2-3 fold higher than baseline nAb titers in RSV vaccine-naïve older adults from other clinical trials and is consistent with the previously reported results for AREXVY at 2-3 years following the initial dose (1)

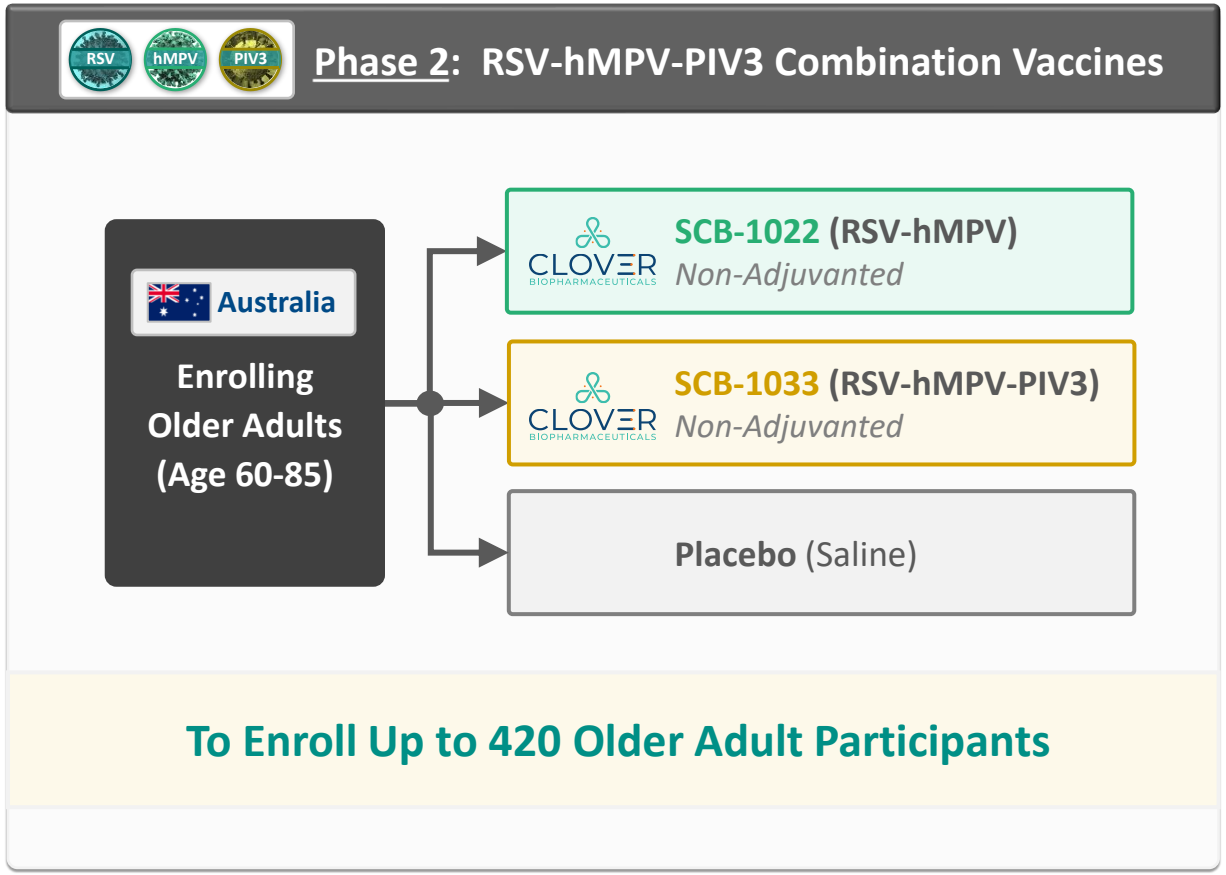
Notes: Clover preliminary results. Geometric mean fold rises (GMFRs) for 1-month post-vaccination versus baseline titers shown for RSV neutralizing antibody titers (±95% confidence intervals).
(1) GSK ACIP Presentation (April 16th 2025).

CLOVER BIOPHARMACEUTICALS

Phase 2 Trial Initiated in Jan 2026; Strengthens First-in-Class Positioning

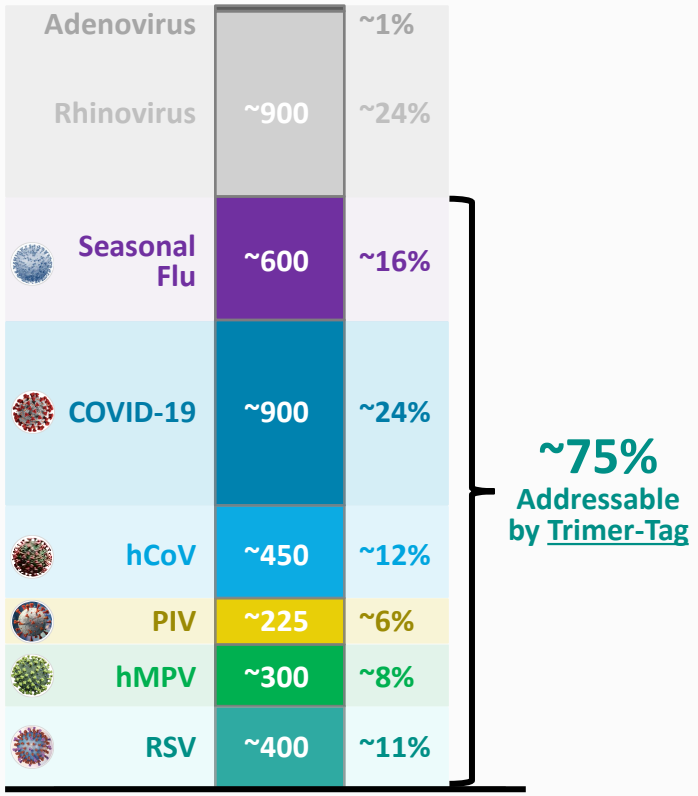
Australia Phase 2

- ☑ Phase 2 Initiation in January 2026 Strengthens Clover's First-in-Class Potential
- ☑ First-Ever RSV-hMPV-PIV3 Combination Vaccine Candidate to Advance to Phase 2
- ☐ Phase 2 Results in 2026 (Immunogenicity & Safety)



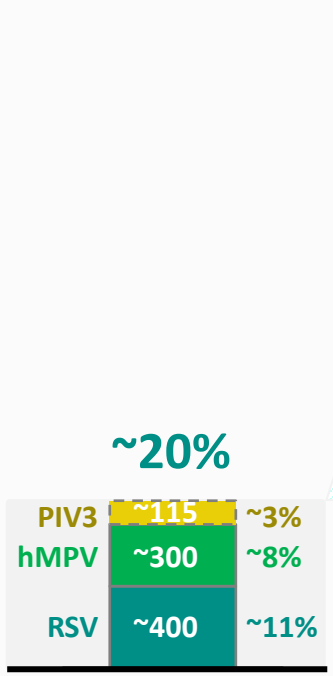
Trimer-Tag Platform has Potential To Address ~75% of Viral Respiratory Disease Burden in Elderly

Annual Disease Burden of Respiratory Viruses in Elderly Population in U.S.
(Est. Hospitalizations per 100,000 Persons)

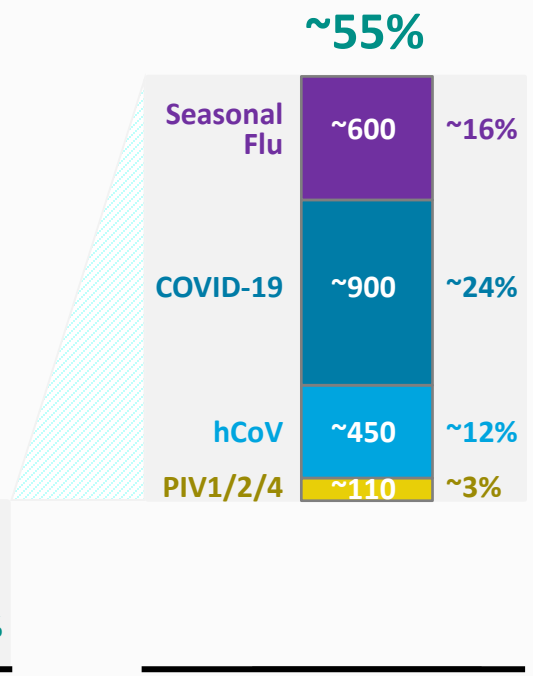


Trimer-Tag Platform Opportunity for Respiratory Combination Vaccines in Elderly

SCB-1022/1033
(Phase 2 Ongoing)



Future Expansion Opportunities



Key Platform Validation & PoC Demonstrated To-Date

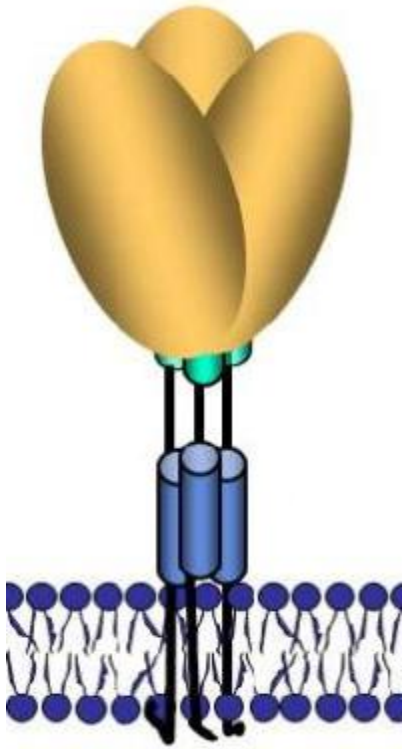
- ☑ **Validated Platform Safety** (40,000+ Doses Administered To-Date)
- ☑ **Validated Platform CMC Commercial Scalability** (2000L DS Scale Achieved for COVID-19, RSV, hMPV, PIV3 Antigens)
- ☑ **No Immune Interference For Combination Vaccines To-Date** (RSV+hMPV±PIV3)
- ☑ **Re-Vaccination/Booster Clinical PoC Demonstrated** (RSV, COVID)
- ☑ **Non-Adjuvanted Clinical PoC Demonstrated** (RSV, hMPV, PIV3)

Note: Illustrative for discussion purposes only and subject to change based on emerging epidemiological data. Disease burden data shown represent approximations for hospitalizations per 100,000 person years in older adults aged 75 years and older in the U.S. in years with a typical outbreak season for each virus (excluding epidemiological data during COVID-19 pandemic affected seasons; excluding epidemiological data for RSV after launch of licensed RSV vaccines).
Abbreviations: RSV (respiratory syncytial virus), hMPV (human metapneumovirus), PIV (parainfluenza virus), hCoV (human coronavirus, including OC43, NL63, HKU1, 229E), PoC (proof-of-concept).
Sources: DOI: 10.1111/irv.12842 | DOI: 10.1001/jamanetworkopen.2024.44756 | DOI: 10.7488/ds/7856 | DOI: 10.3390/pathogens14121277 | DOI: 10.22541/au.175463289.90830107/v1 | CDC ACIP Presentation (06.25.2025) | DOI: 10.1111/irv.13040

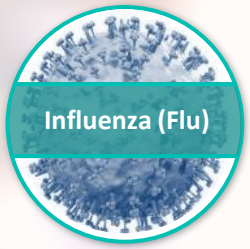
Appendix

Dozens of Trimeric Antigen Targets for Potential Vaccine Development; Differentiated Proof-of-Concept for Trimer-Tag has been Demonstrated for 10+ Viruses

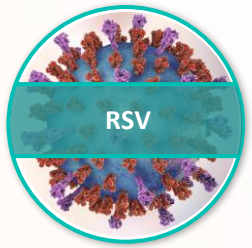
Naturally-trimeric Structure Surface Antigens of Viruses & Pathogens



S antigen



HA antigen



F antigen

gE antigen

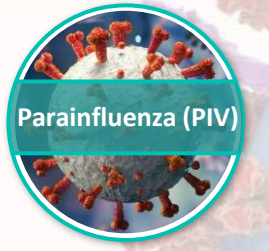
gB antigen

gB antigen

gB antigen

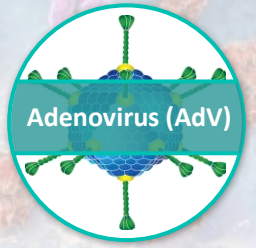
Pgp3 antigen

PorB antigen

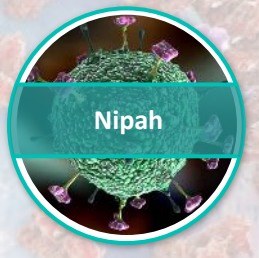


F antigen

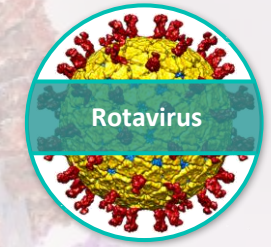
F antigen



Fiber antigen



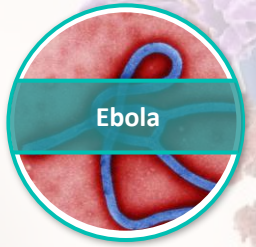
F antigen



VP8 antigen

G antigen

E antigen



GP antigen

GP antigen

F antigen

F antigen

Gp120/41 antigen

CLOVER BIOPHARMACEUTICALS

Trimer-Tag: *Robust Safety Database Established, Including COVID-19 Global Phase 3 Study*

Belgium Brazil Colombia Philippines S. Africa

☑ **No Significant Safety Concerns Identified in COVID-19 (SCB-2019 + CpG 1018/Alum) Global Phase 2/3 Study in >15,000 Subjects Receiving >30,000 Doses**

Vaccine 41 (2023) 2353–2360

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Six-month safety follow-up of an adjuvanted SARS-CoV-2 trimeric S-protein subunit vaccine (SCB-2019) in adults: A phase 2/3, double-blind, randomized study

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ABSTRACT

Background: We evaluated the safety of SCB-2019, a protein subunit vaccine candidate containing a recombinant SARS-CoV-2 spike (S) trimer fusion protein, combined with CpG-1018/alum adjuvants.
Methods: This ongoing phase 2/3, double-blind, placebo-controlled, randomized trial is being conducted in Belgium, Brazil, Colombia, the Philippines, and South Africa in participants ≥ 12 years of age. Participants were randomly assigned to receive 2 doses of SCB-2019 or placebo administered intramuscularly 21 days apart. Here, we present the safety results of SCB-2019 over the 6-month period following 2-dose primary vaccination series in all adult participants (≥18 years of age).
Results: A total of 30,137 adult participants received at least one dose of study vaccine (n = 15,070) or placebo (n = 15,067) between 24 March 2021 and 01 December 2021. Unsolicited adverse events, medically-attended adverse events, adverse events of special interest, and serious adverse events were reported in similar frequencies in both study arms over the 6-month follow-up period. Vaccine-related SAEs were reported by 4 of 15,070 SCB-2019 recipients (hypersensitivity reactions in two participants, Bell's palsy, and spontaneous abortion) and 2 of 15,067 placebo recipients (COVID-19, pneumonia, and acute respiratory distress syndrome in one participant and spontaneous abortion in the other one). No signs of vaccine-associated enhanced disease were observed.
Conclusions: SCB-2019 administered as a 2-dose series has an acceptable safety profile. No safety concerns were identified during the 6-month follow-up after the primary vaccination.
Clinical Trials Registration: NCT04672395; EudraCT: 2020-004272-17.

1. Introduction

The severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) pandemic has mobilized the global scientific community to develop effective vaccines for preventing coronavirus infectious disease caused by SARS-CoV-2 (COVID-19) [1,2]. A total of 41 vaccines against COVID-19 have been approved by Health Authorities in at least one country and 11 of them were granted emergency use authorization by World Health Organization [3]. As of 13 September 2022, more than 12.6 billion doses of COVID-19 vaccines have been administered around the world [4]. Various technologies have been employed to develop these vaccines, including inactivated and recombinant subunit protein vaccines, viral vector-based vaccines, and mRNA vaccines [5]. Due to the accelerated, global, multi-manufacturer development of COVID-19 vaccines, it is crucial that vaccine safety assessment including monitoring, investigation, and analysis is done throughout the life cycle of vaccine development in a harmonized and standardized manner [6]. The Safety Platform for Emergency vACcines (SPEAC) and the Brighton Collaboration have identified potential adverse events of special interest (AESIs) relevant to the development of COVID-19 vaccines [7,8]. Some of these AESIs have been previously identified with immunization in general (e.g., anaphylaxis, Guillain-Barré syndrome [GBS]), whereas some are relevant to certain vaccine platforms, and others are specific to COVID-19 vaccines (e.g., myocarditis, pericarditis) [9].

Most of the known side effects of COVID-19 vaccines are mild and short lived [10–14]. However, during clinical trials and through the safety monitoring systems, a few medically significant

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☑ **Similar Frequencies Observed in Both Study Arms During the 6-month Follow-Up Period for:**
Unsolicited adverse events (**AEs**), medically-attended adverse events (**MAAEs**), adverse events of special interest (**AESIs**), and serious adverse events (**SAEs**) were reported

Safety Overview During 6-Month Follow-Up Period

Adverse events	SCB-2019 (CpG 1018/Alum) (N = 15,070)		Placebo - Saline (N = 15,067)	
	n_s (n_e)	% (95 % CI)	n_s (n_e)	% (95 % CI)
Any unsolicited adverse events	2497 (4132)	16.6 (16.0–17.2)	2597 (4419)	17.2 (16.6–17.8)
Related to vaccination	712 (1057)	4.7 (4.4–5.1)	480 (645)	3.2 (2.9–3.5)
Severe	73 (93)	0.5 (0.4–0.6)	93 (144)	0.6 (0.5–0.8)
Any medically-attended adverse events	1071 (1697)	7.1 (6.7–7.5)	1211 (1910)	8.0 (7.6–8.5)
Any serious adverse events	90 (114)	0.6 (0.5–0.7)	114 (176)	0.8 (0.6–0.9)
Related to vaccination	4 (4)	0.0 (0.0–0.1)	2 (4)	0.0 (0.0–0.0)
Any adverse events of special interest	323 (509)	2.1 (1.9–2.4)	496 (791)	3.3 (3.0–3.6)
Related to vaccination	12 (12)	0.1 (0.0–0.1)	13 (14)	0.1 (0.0–0.1)
Any adverse events leading to early study termination	9 (10)	0.1 (0.0–0.1)	23 (29)	0.2 (0.1–0.2)
Death	9 (9)	0.1 (0.0–0.1)	23 (29)	0.2 (0.1–0.2)

Abbreviations: CI, confidence interval.
N is the number of participants in the study arm used as denominator for percentage calculation; n_e is the number of events; n_s is the number of participants reporting the adverse event (AE).
For a participant reporting greater than 1 AE for a given symptom within 7 days post-vaccination, the most severe AE was included in the calculation of percentage.
A related AE was an AE that was considered to be probably or possibly caused by the study vaccination.

Source: DOI: 10.1016/j.vaccine.2023.02.018

CLOVER BIOPHARMACEUTICALS

Trimer-Tag: *Robust Safety Database Established, Including COVID-19 Global Phase 3 Study*

Belgium Brazil Colombia Philippines S. Africa

☑ No Significant Safety Concerns Identified in COVID-19 (SCB-2019 + CpG 1018/Alum) Global Phase 2/3 Study in >15,000 Subjects Receiving >30,000 Doses

Adverse Events of Special Interest (AESIs) Reported by ≥2 Participants in Any Group by System Organ Class & Preferred Term

Adverse event of special interest	SCB-2019 (CpG 1018/Alum) (N = 15,070)		Placebo - Saline (N = 15,067)	
	n_s (n_e)	% (95 % CI)	n_s(n_e)	% (95 % CI)
Any adverse event of special interest	323 (509)	2.1 (1.9–2.4)	496 (791)	3.3 (3.0–3.6)
Cardiac disorders	7 (7)	0.0 (0–0.1)	2 (2)	0.0 (0–0.0)
Sinus tachycardia	2 (2)	0.0 (0–0)	0 (0)	0.0 (0–0)
Tachycardia	2 (2)	0.0 (0–0)	0 (0)	0.0 (0–0)
Immune system disorders	6 (6)	0.0 (0–0.1)	6 (6)	0.0 (0–0.1)
Hypersensitivity	6 (6)	0.0 (0–0.1)	4 (4)	0.0 (0–0.1)
Anaphylactic reaction	0 (0)	0.0 (0–0)	2 (2)	0.0 (0–0)
Infections and infestations	1 (1)	0.0 (0–0)	3 (4)	0.0 (0–0.1)
Sepsis	0 (0)	0.0 (0–0)	2 (2)	0.0 (0–0)
Metabolism and nutrition disorder	4 (4)	0.0 (0–0.1)	5 (5)	0.0 (0–0.1)
Gout	3 (3)	0.0 (0–0.1)	4 (4)	0.0 (0–0.1)
Musculoskeletal and connective tissue disorder	2 (2)	0.0 (0–0)	3 (3)	0.0 (0–0.1)
Gouty arthritis	2 (2)	0.0 (0–0)	2 (2)	0.0 (0–0)
Nervous system disorders	288 (473)	1.9 (1.7–2.1)	463 (745)	3.1 (2.8–3.4)
Anosmia	251 (252)	1.7 (1.5–1.9)	384 (386)	2.5 (2.3–2.8)
Ageusia	199 (201)	1.3 (1.1–1.5)	326 (327)	2.2 (1.9–2.4)
Hyposmia	4 (4)	0.0 (0–0.1)	9 (9)	0.1 (0–0.1)
Parosmia	4 (4)	0.0 (0–0.1)	7 (7)	0.0 (0–0.1)
Hypogeusia	3 (3)	0.0 (0–0.1)	9 (9)	0.1 (0–0.1)
Agnosia	2 (2)	0.0 (0–0)	2 (2)	0.0 (0–0)
Taste disorder	2 (2)	0.0 (0–0)	2 (2)	0.0 (0–0)
Bell's palsy	2 (2)	0.0 (0–0)	0 (0)	0.0 (0–0)
Seizure	2 (2)	0.0 (0–0)	0 (0)	0.0 (0–0)
Renal and urinary disorders	0 (0)	0.0 (0–0)	3 (3)	0.0 (0–0.1)
Acute kidney injury	0 (0)	0.0 (0–0)	3 (3)	0.0 (0–0.1)
Respiratory, thoracic and mediastinal disorders	2 (2)	0.0 (0–0)	6 (6)	0.0 (0–0.1)
Acute respiratory distress syndrome	1 (1)	0.0 (0–0)	3 (3)	0.0 (0–0.1)
Acute respiratory failure	0 (0)	0.0 (0–0)	2 (2)	0.0 (0–0)
Skin and subcutaneous tissue disorders	12 (13)	0.1 (0–0.1)	13 (14)	0.1 (0–0.1)
Urticaria	9 (10)	0.1 (0–0.1)	6 (7)	0.0 (0–0.1)
Alopecia	1 (1)	0.0 (0–0)	2 (2)	0.0 (0–0.1)

N is the number of participants in the study arm used as the denominator for calculating percentages; n_e is the number of events; n_s is the number of participants reporting the adverse event.
Serious adverse events were collected up to the cutoff date for safety analysis (01 December 2021).
Adverse events were coded using MedDRA version 24.1 mixed.

→ No Imbalances in Overall AESIs

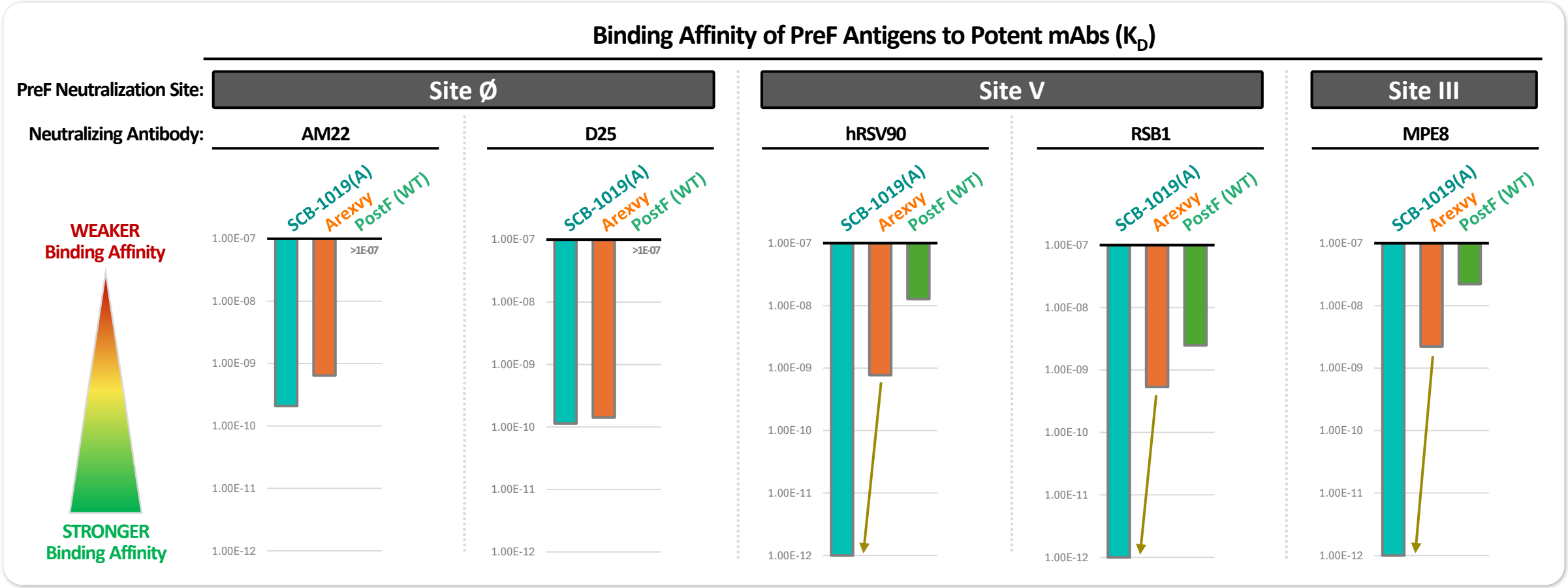
→ No Imbalances in Immune-Related AESIs

Source: DOI: 10.1016/j.vaccine.2023.02.018

CLOVER BIOPHARMACEUTICALS

Preclinical Data (mAb Binding Affinity): Clover RSV PreF (SCB-1019) Versus GSK (AREXVY)

☑ **Clover's RSV PreF Demonstrates Differentiated and Stronger Binding Affinity than GSK (AREXVY) Against mAbs at Highly Potent Neutralization Sites (Site V, Site III)**



Note: Clover preclinical. K_D (Dissociation Constant) measured by ForteBio assay.

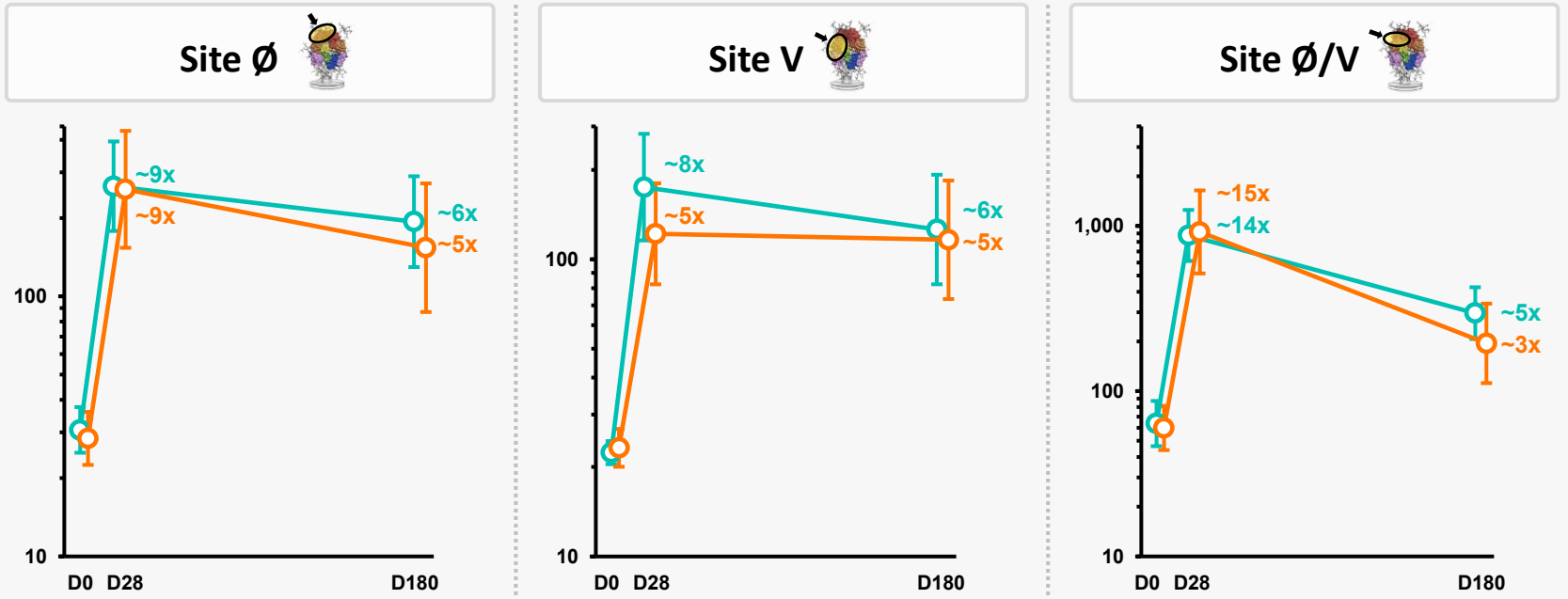
Prior Phase 1 Clinical Validation of Clover's RSV PreF (SCB-1019) Versus GSK (AREXVY) – Oct 2024

Aus Ph1 (2024)

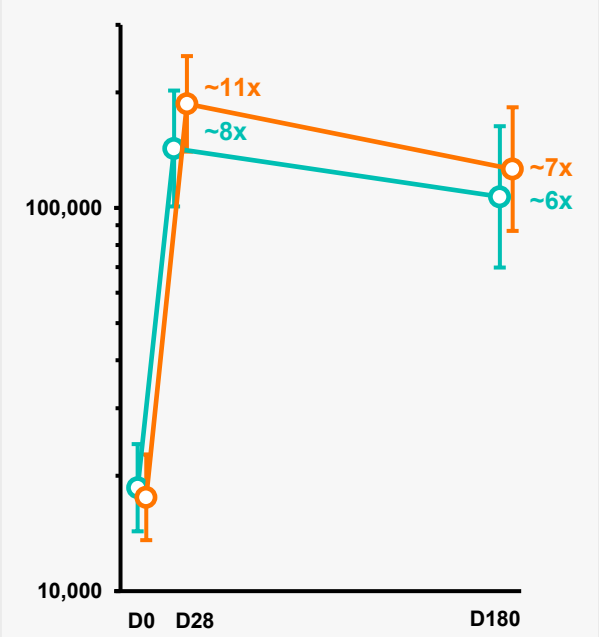
☑ SCB-1019 Elicited Durable Site Ø/V-Specific NAb Responses + Observed Trend in Fewer Binding (Non-Neutralizing) Antibodies

Note: **Sites Ø+V** Comprise **>60% of Highly-Potent RSV Neutralizing Antibody Repertoire** in Humans [1]

NAb Site-Specific Competitive ELISA Titers (GMT)



Total PreF Binding Antibodies (GMT)



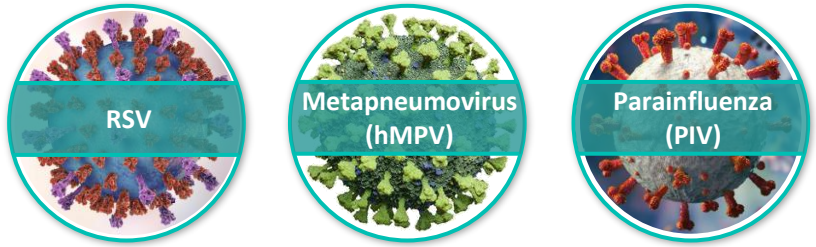
Clover (SCB-1019) - *Non-Adjuvanted* (n=30)
GSK (AREXVY) - *AS01-Adjuvanted* (n=30)

Note: Dots represent Bars represent GMTs (±95% confidence intervals). GMFRs for Day 28 and Day 180 versus Baseline (Day 0) are denoted next to the dots.
Preliminary results shown for ELISA assays (exploratory study objectives). Competitive ELISAs utilizing highly-potent neutralizing mAbs against Site Ø (RSV-A/B cross-reactive), Site V (RSV-B preferred) and overlapping Site Ø/V (RSV-A preferred).
Abbreviations: GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise), NAb (Neutralizing Antibody), mAb (Monoclonal Antibody).
(1) DOI: 10.1126/sciimmunol.aaj1879. Highly-potent RSV NAbs defined as neutralization potency (IC_{50}) < 50ng/mL.

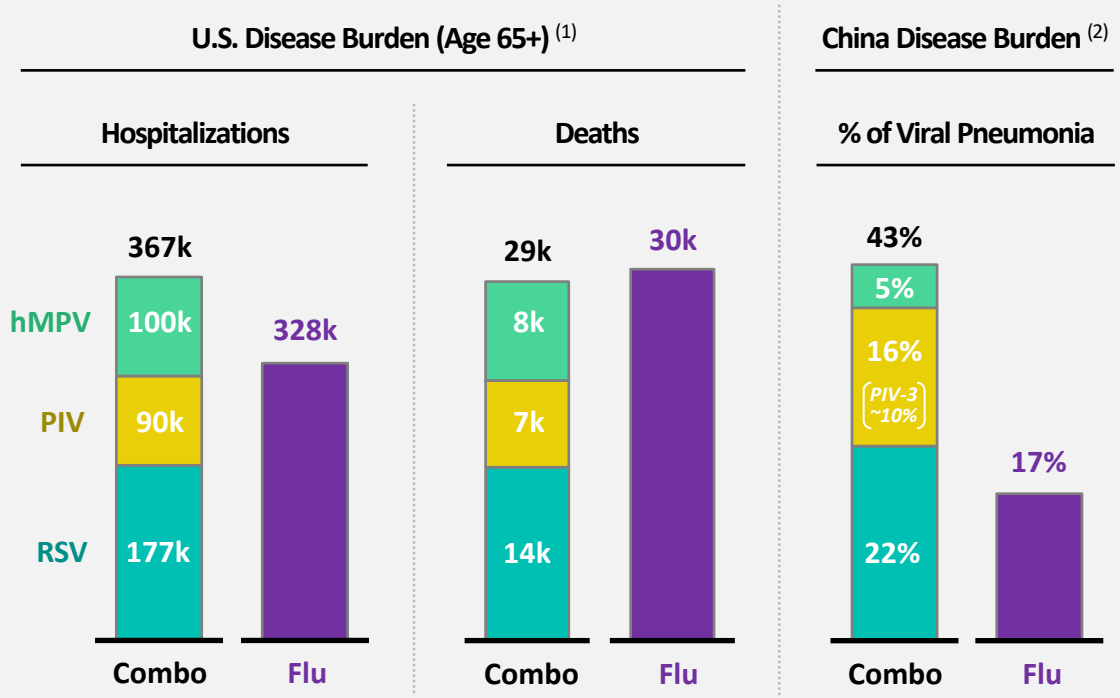
CLOVER BIOPHARMACEUTICALS

Respiratory PreF Combo Vaccine (RSV + hMPV + PIV) Opportunity

- **Total Disease Burden of Combo (RSV+hMPV+PIV) is similar or greater than Flu Globally;** combination vaccine is a compelling opportunity & unmet need
- **Directly leveraging Clover's RSV experience to develop 'Respiratory Combo Vaccines' across mononegavirales order of viruses (RSV + hMPV ± PIV)**
- **Trimer-Tag protein subunit has platform advantages for combo versus mRNA (combo dose is limited by safety) and VLPs (complicated CMC)**



Virus Order/ Disease	☑ Mononegavirales Order of Viruses ☑ Symptomatic Respiratory Disease, Including LRTD
PreF Antigen	☑ All 3 have Similar Trimeric Fusion (F) Antigen, Requiring Stabilization in Prefusion form (PreF)
Seasonality	☑ All 3 Observe Seasonal Outbreaks in Winter/Spring
At-Risk Populations	☑ Highest Risk Populations are Elderly and Infants



☑ **Total Disease Burden of Combo (RSV+hMPV+PIV3) is Similar or Greater than Flu Globally**

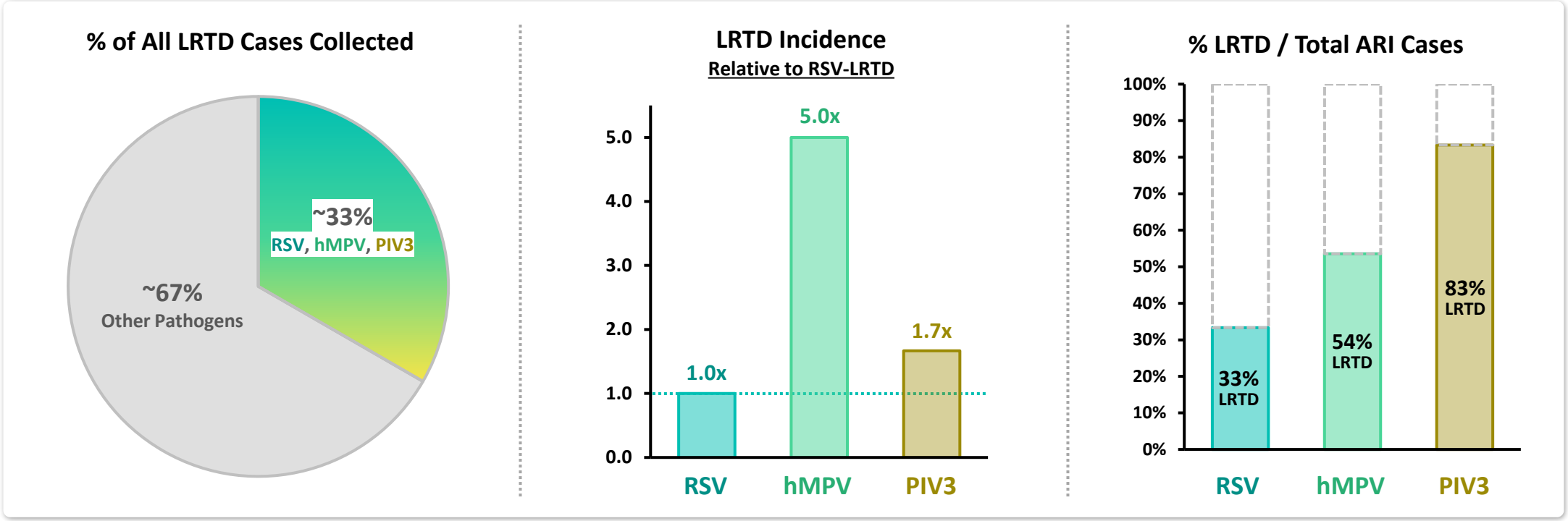
(1) Sources: **[A]** Widmer et al., 2012; **[B]** Russell et al., 2019 (62% of RSV); **[C]** Colosia et al., 2017; **[D]** Using RSV rate from Colosia 2017 as proxi. **[E]** https://www.cdc.gov/rsv/research/us-surveillance.html **[F]** Compilated data from CDC, 9 seasons from 2010-2011 to 2018-2019 https://www.cdc.gov/flu/about/burden/index.html **[G]** Burden in already vaccinated pop **[H]** Assuming vaccine durability >1 year.

(2) Li et al., Nat. Commun., 2021 (DOI: 10.1038/s41467-021-25120-6). Data across all age groups from 2009-2019.

CLOVER BIOPHARMACEUTICALS

Clover-Sponsored Epidemiology Pilot Study in China ('24-'25 Season)

- Pilot Study Enrolled ~1,100 Children Aged 2-5 Years in 2 Provinces (Northern China + Southern China)
- Surveillance for PCR-Confirmed Symptomatic ARI and LRTD from ~OCT-2024 to ~APR-2025



☑ ~8x Combined Disease Burden Observed in Epi Study for RSV + hMPV + PIV3 (vs RSV Alone)

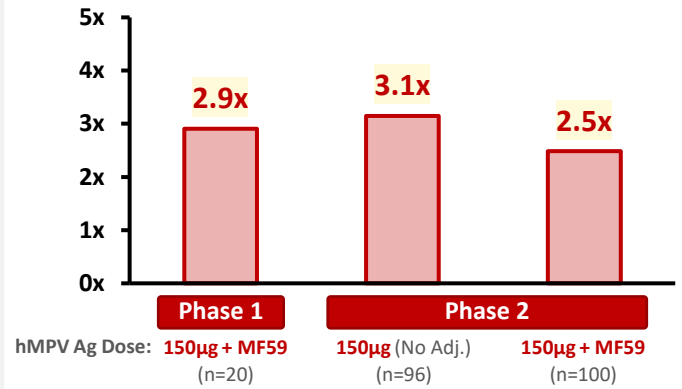
☑ Clover Plans to Conduct a Larger Epi Study During the Upcoming '25-'26 Season

Note: Preliminary interim epidemiology study results (non-QC'd).
Abbreviations: ARI (Acute Respiratory Infection); LRTD (Lower Respiratory Tract Disease).
Source: Clover-sponsored pilot epidemiology study in China (surveillance from ~OCT-2024 to ~APR-2025).

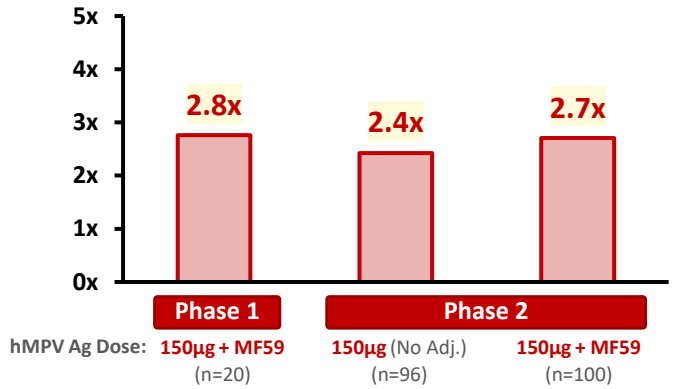
AstraZeneca (Icosavax) IVX-A12 (RSV-hMPV Combo) – Phase 1/2 Results for hMPV NAbs

- IVX-A12 (RSV-hMPV Combo) Induced ~2.5-3.1x GMFRs in hMPV-A NAbs and ~2.4-2.8x GMFRs in hMPV-B NAbs in Phase 1 and Phase 2 Clinical Trials in Older Adults
- These Phase 1/2 Results in Older Adults were Supportive of AZ's up to $1.1 Billion Acquisition of Icosavax in December 2023

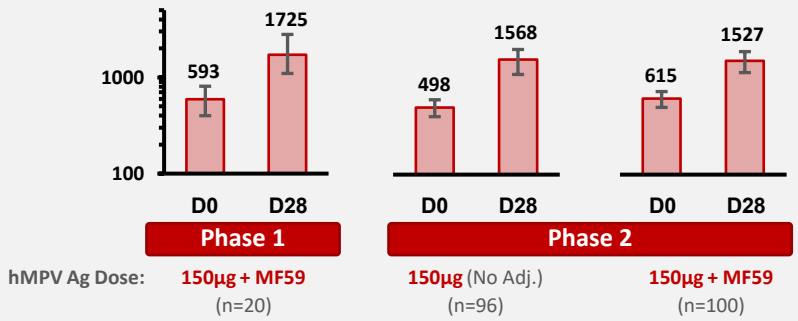
hMPV-A NAb – GMFR (Day 28/Day 0)



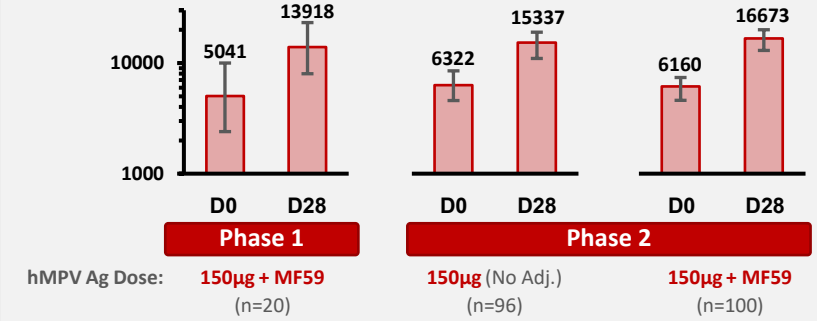
hMPV-B NAb – GMFR (Day 28/Day 0)



hMPV-A NAb – Geometric Mean Titers (GMT)



hMPV-B NAb – Geometric Mean Titers (GMT)



IVX-A12 GMFRs for RSV NAbs (~3-6x) Compared to hMPV NAbs (~2.5-3x) Suggest that Absolute hMPV GMFRs May Naturally be Lower Than RSV GMFRs

Note: GMFRs for Day 28 versus Baseline (Day 0) are shown. Bars represent geometric means (±95% confidence intervals).
Abbreviations: GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise), NAb (Neutralizing Antibody).
Sources: IVX-A12 Phase 1 Results (DOI: 10.1093/ofid/ofaf160); IVX-A12 Phase 2 Results (ISIRV RSV Symposium Presentation in MAR-2025 | NCT05903183).

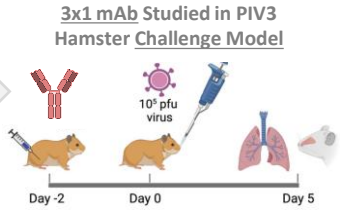
CLOVER BIOPHARMACEUTICALS

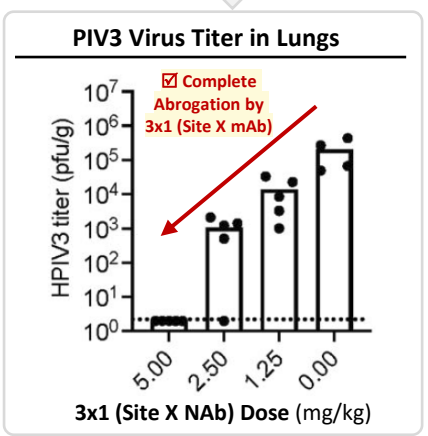
PIV3 Neutralizing Antibodies – Background & Overview of Published Peer-Reviewed Literature

- PIV3 HN Antibodies are Immuno-Dominant in Baseline (Unvaccinated) Human Sera (Low Levels of PIV3 PreF Neutralizing Antibodies are Detected in Baseline [Unvaccinated] Human Sera)
- However, PIV3 PreF Antibodies (if Induced) are Highly Neutralizing, and the PreF Hypothesis has been Validated by RSV PreF Vaccines

☑ PIV3 PreF-Specific NAbs are Highly Potent & Can Completely Abrogate PIV3 in Challenge Models (1)

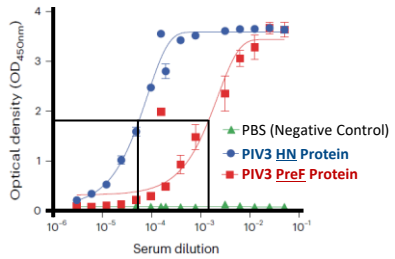
3x1 is a PIV3 PreF (Site X) Highly-Potent Neutralizing Antibody





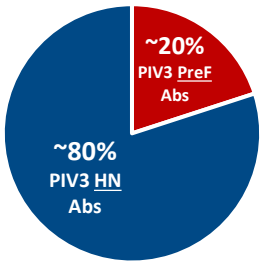
Majority of PIV3 Antibody Signal in Baseline (Unvaccinated) Human Sera are PIV3 HN Antibodies

Binding of PIV3 HN/PreF Antigens to Antibodies in Baseline Human Sera (2)



>10-Fold Higher Level of PIV3 HN Binding Antibodies Compared to PIV3 PreF Abs in Baseline Human Sera

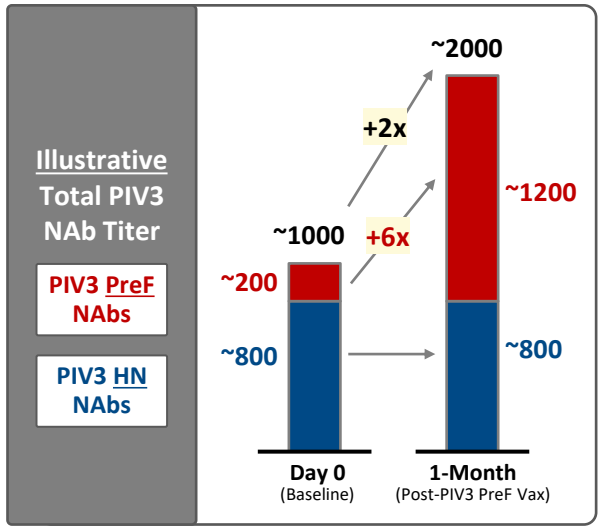
Isolation of PIV3 Neutralizing Abs from Human Memory B Cells (2,3)



Majority (~80%) of PIV3 NAbs Isolated from Human Donor are PIV3 HN; Minority (~20%) are Against PIV3 PreF

Highly Illustrative Interpretation & Framework

Implies that a ~2x GMFR in Total PIV3 NAbs Induced by a PIV3 PreF Vaccine May Represent ≥6x GMFR in PIV3 PreF-Specific PIV3 Nabs



Abbreviations: GMFR (Geometric Mean Fold Rise), NAb (Neutralizing Antibody).

(1) DOI: 10.1038/s41467-023-36459-3
(2) DOI: 10.1038/s41564-024-01722-w
(3) Panel of 4 PIV3 HN NAbs and 1 PIV3 PreF NAb isolated from a human PBMC donor.

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