



Differentiated & Potential Best-in-Class Bivalent RSV Vaccine Candidate (SCB-1019):

Program Overview & Data Update

January 2025

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.



RSV Vaccines: Blockbuster Market Validated, With Significant Expansion Opportunities

Global RSV Vaccine Addressable Market

(Illustrative Estimated Relative Market Sizes)

Current Market

(Approved Indications)



Expected Future Expansion

Young Kids

(Age 2-5)

Significant Untapped Market Expansion Opportunities Requiring Platform & Product Differentiation



~\$2.5 Billion Sales
1st Year of Launch (1)

RSV Vaccines is the Fastest (Non-Pandemic) Vaccine in History to Reach Blockbuster Status

> Older Adults Re-Vaccination (Age ≥60)



- High Disease-Burden for RSV in Young Kids Versus Older Adults Based on Epi Data
- Untapped Opportunity: Field is in Early-to-Mid Stage (Pfizer Ph1 / Moderna Ph2)
- Largest Addressable Market: Re-vaccination to Drive Recurrent Sales from Each Vaccinee in Large Older Adult & Elderly Population Pool Globally (Similar to Seasonal Flu Vaccines)
- Need for Re-Vaccination & Interval: Proteinbased RSV Vaccines Appear to Have Durable Efficacy for ~2 Seasons, Indicating Need for Revaccination Every ~2 Years
- Opportunity for New Players: GSK/Pfizer Revaccination Data has been Unsuccessful to-date (Potentially Due in Part to T4-Foldon Tag Inducing Immune Interference); Large Opportunity for New Players if Re-vaccination Issues can be Overcome

Other

Maternal Immunization, High-Risk/Co-Morbidities (18-59 Years)

Older Adults
Initial Dose
(Age ≥60)

Older Adults
Initial Dose
(Age ≥60)



- ✓ Validated Market: ~\$2.5Bn Sales in 1st Year of Launch; ex-U.S. Markets Still Largely Untapped
- After prevalent population penetrated, 'initial dose' market to be mainly comprised of people newly-entering the age cohort each year







RSV-Containing Respiratory Combination Vaccines

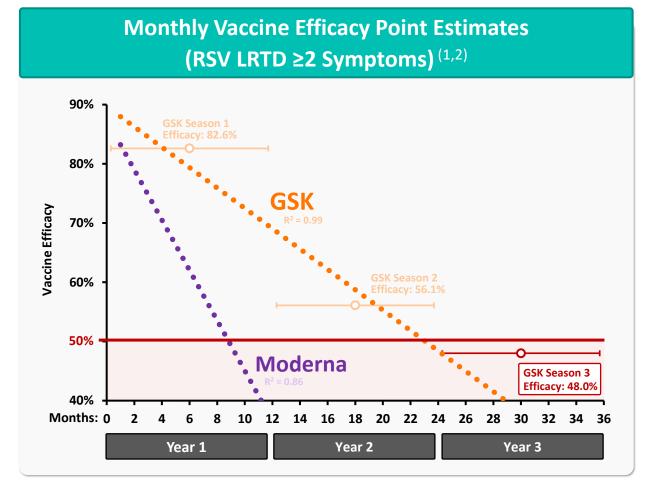
- RSV + hMPV ± PIV-3: Could be Combined with RSV; Belong to Same Mononegavirales Order as RSV, with Trimeric PreF Antigens; Slight Seasonality Differences May Not be an Issue if Protein Vaccine Durability is ~2 Years
- Respiratory Combination Vaccines are Expected to Take Significant Future Market Share, Given Broader Coverage & Convenience if Successfully Developed
- Many LCM Precedents for Combination, Higher-Valency, or Improved Vaccines Taking Majority Market Share (>60%), Including Pediatric Combo vs DTaP, HPV9 vs HPV2/4, Seasonal Flu QIV vs TIV, RotaTeq vs Rotarix, MenACWY vs MenC, PCV vs PPSV
- Protein Subunit Platform Advantage:

 Favorable Safety & Tolerability Profile of
 Protein Subunits Enables Combining
 Multiple Antigens (mRNA May be Limited by
 Reactogenicity), and VLP has Complicated
 CMC (Requires Multiple Components)



Efficacy of Protein-Based RSV Vaccines is Durable for ~2 Seasons, But Re-Vaccination is Needed

- Protein-Based RSV Vaccines Appear to have Durable Efficacy Compared to mRNA, with GSK (AREXVY) Reporting the Highest Vaccine Efficacy & Longest Durability To-Date
- However, Re-Vaccination is Still Needed to Boost and Sustain Protection (Similar to Flu & COVID);
 GSK's Efficacy Wanes & Falls to ~43-48% in Year 3 (3)
- Indicates Potential Optimal <u>Re-Vaccination Interval</u> of ~2 Years for Protein-Based RSV Vaccines



Note: Cross Trial Comparisons for Illustrative Purposes Only (Efficacy endpoints are different across vaccines and studies).

Sources: ACIP Meetings including 21 JUNE 2023 (GSK Presentations), 29 FEB 2024 (Moderna Presentation), 26 JUNE 2024 (GSK and Moderna Presentations). 08 OCT 2024 GSK Press Release.

- (1) Primary Endpoints: GSK (RSV-LRTD ≥2 Symptoms/Signs for ≥24 Hours), Moderna (RSV-LRTD ≥2 Symptoms).
- Linear Regression (VE Primary Endpoints)
- GSK (Y = -0.0086x + 0.8883) | Moderna (Y = -0.0212x + 0.8535).
- 3) 43% vaccine efficacy point estimate in year 3 for prevention of severe RSV disease. 48% vaccine efficacy point estimate in year 3 for prevention of RSV LRTD ≥2 Symptoms/Signs

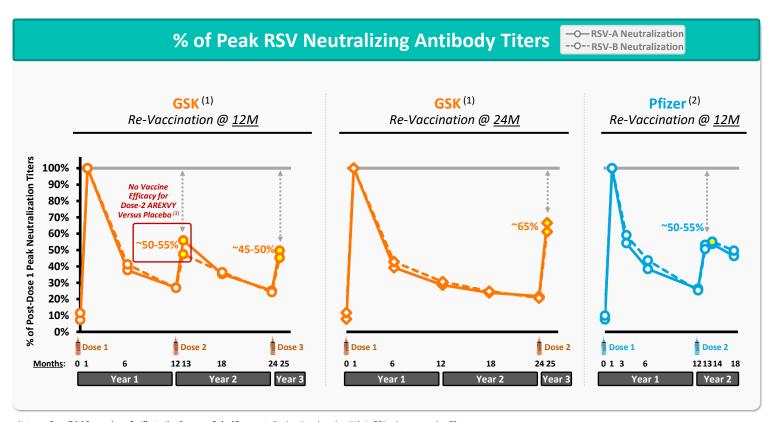


BUT, Re-Vaccination Issues Encountered for GSK & Pfizer RSV Vaccines

GSK (AREXVY) / Pfizer (ABRYSVO)

- Re-Vaccination at 1-2 Year Intervals Only Boosts RSV
 Neutralizing Antibodies Back to ~45-65% of Peak Levels
- ➢ GSK/Pfizer are Evaluating Re-Vaccination at 3-5 Year Intervals, but Efficacy Data Indicates Optimal Interval is ~2 Years
- RSV PreF Both Utilize <u>T4-Foldon Trimerization Tag</u> (Which Induces Immune Response in Humans); Could Potentially Cause Immune-Interference Upon Re-Vaccination?
 - Moderna (4) & AstraZeneca (Icosavax) (5) do not appear to suffer from the same re-vaccination issues to-date

Clover's Trimer-Tag (Immuno-Silent in Humans)
May Enable More Effective Re-Vaccination



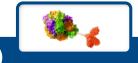
Note: Cross Trial Comparisons for Illustrative Purposes Only. Pfizer neutralization titers based on IU/mL. GSK units expressed as ED₆₀.

Sources: (1) GSK ACIP Presentation (26-JUN-2024), (2) Pfizer 2023 VRBPAC Company Briefing Document, (3) 21 JUNE 2023 ACIP Meeting (GSK Presentation). Based on primary efficacy endpoint (RSV-LRT ≥2 Symptoms/Signs). (4) Moderna ACIP Presentation (29-FEB-2024), (5) Icosavax Company Presentation IVX-121 (28-JUN-2023).



SCB-1019 has a De-Risked & Potential Best-in-Class Combined Efficacy & Safety Profile, with Potential

<u>Differentiation</u> to Address Unmet Needs in the Global RSV Vaccine Market (<u>Re-Vaccination</u> & <u>Combo</u>)



(1)

Top-Tier PreF & De-Risked Potential Vaccine Efficacy

- ☑ RSV neutralizing antibodies for Clover's Non-Adjuvanted SCB-1019 matched GSK's ASO1_E-adjuvanted AREXVY in older adults in a head-to-head Phase 1 clinical trial
- ✓ Proprietary stabilizing mutations & Trimer-Tag platform technology utilized for SCB-1019; confirmed as stable PreF-Trimer



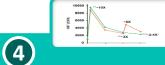
Immunological Breadth (Bivalent RSV-A + RSV-B)

- ✓ SCB-1019 Bivalent RSV-A/B induces broad neutralization against both RSV-A & RSV-B, demonstrated in Phase 1 clinical trials (including potent RSV-B specific neutralizing antibodies)
- ✓ Monovalent RSV-A vaccines (observed suboptimal breadth & durability trends against RSV-B in clinical trials to-date (1)



Potential Best-in-Field Safety & Tolerability

- ✓ SCB-1019 has demonstrated a potential best-in-field safety & tolerability profile in Phase 1 clinical trials, including significantly better local tolerability than GSK
- Safety & tolerability important to maximizing vaccine uptake, especially in certain countries and in young children



RSV Re-Vaccination Ability (No Immune Interference)

- ☑ Trimer-Tag (immuno-silent in humans) may enable more effective revaccination; boostability demonstrated for COVID-19 vaccine
- ✓ GSK observed lack of efficacy after a second dose in Phase 3 study (with suboptimal increases in RSV neutralizing antibody levels); similar challenge observed for Pfizer (Abrysvo)



RSV-Containing Respiratory
Combo Vaccine

- ✓ SCB-1019 (RSV) is being utilized to develop Respiratory Combination Vaccines across Mononegavirales order of viruses (RSV + hMPV ± PIV3)
- ✓ Directly leveraging Clover's validated
 Trimer-Tag platform and PreF
 stabilization experience

✓ <u>Head-to-Head Clinical Results</u> Versus <u>GSK (AREXVY)</u> De-Risks & Indicate Clover's <u>Potential Best-in-Class Combined Efficacy & Safety Profile</u> for SCB-1019 (Non-Adjuvanted Bivalent RSV-A/B Vaccine Candidate)

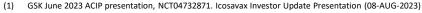


2025: Planned to <u>Initiate Clinical Trials</u> to Evaluate

<u>SCB-1019</u> in an <u>RSV Re-Vaccination Setting</u>

and as Part of a <u>Respiratory Combination Vaccine</u>



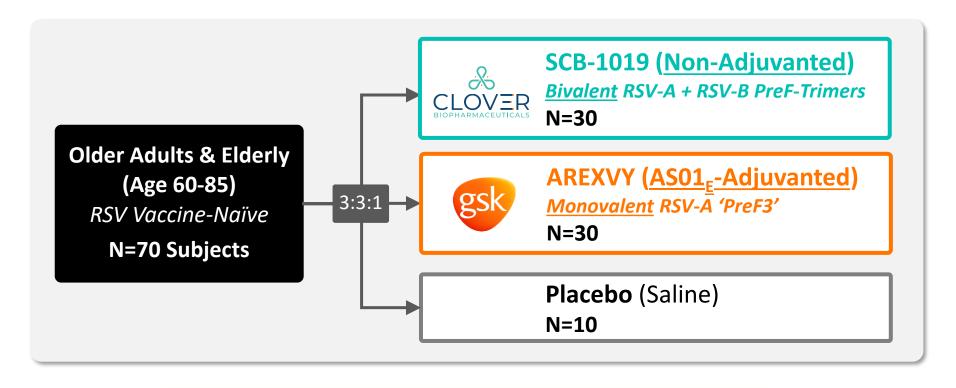






Clover SCB-1019 Phase 1: Study Design

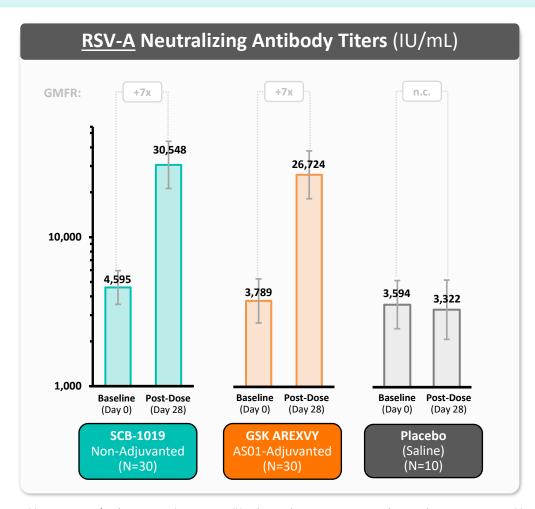
- ✓ 70 Older Adult Subjects (Age 60-85) Enrolled to Receive Non-Adjuvanted SCB-1019, AS01_E-Adjuvanted AREXVY, or Placebo
- ☑ Study Follows Previously Announced Positive Phase 1 Safety & Immunogenicity Results for SCB-1019 in 48 Older Adult Subjects

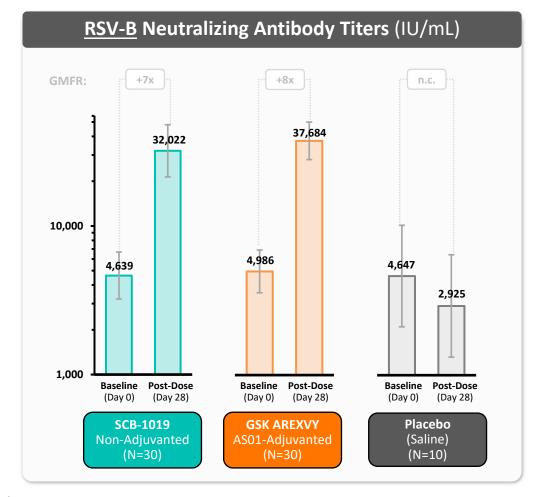




Clover SCB-1019 Phase 1: Immunogenicity Results

RSV Neutralizing Antibody Titers for Clover's Non-Adjuvanted SCB-1019 Matched GSK's AS01-Adjuvanted AREXVY in RSV-Vaccine Naïve Older Adults (Aged 60-85 Years) at 28 Days Post-Vaccination



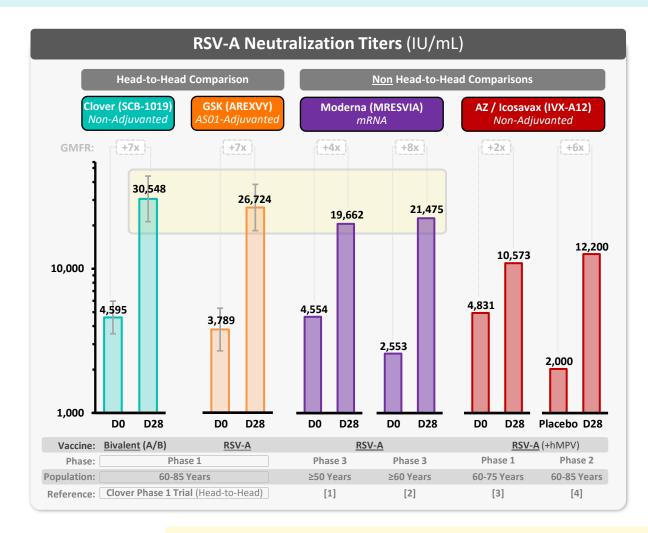


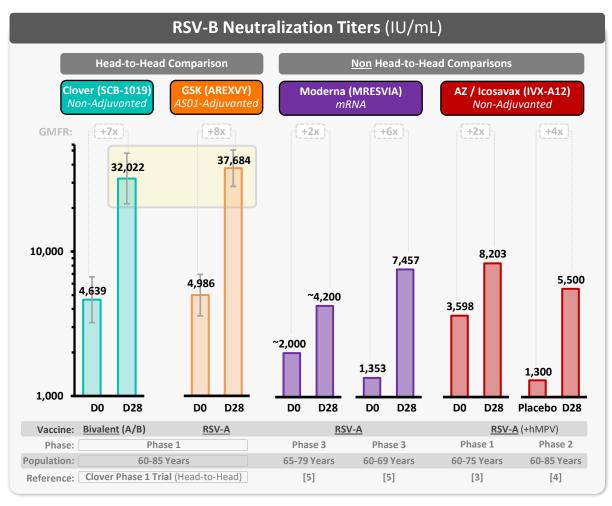
Abbreviations: <u>IU/mL</u> (International Units Per Milliliter), <u>GMT</u> (Geometric Mean Titer), <u>GMFR</u> (Geometric Mean Fold Rise). Note: Bars represent GMTs (± 95% confidence intervals).

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.



SCB-1019 Immunogenicity in Older Adults is In-Line or Potentially Favorable to Other RSV PreF Vaccines





☑ Potential <u>Top-Tier Vaccine Efficacy</u> of SCB-1019 has been <u>Significantly De-Risked</u>

Note: Cross Trial Comparisons for Illustrative Purposes Only. RSV neutralization titers expressed as IU/mL calculated using comparison to NIBSC 16/284 reference sera (testing was conducted at different laboratories across clinical trials). Bars represent GMTs (± 95% confidence intervals) Abbreviations: IU/mL (International Units Per Millilliter), GMT (Geometric Mean Field Rise).

RIM Address ACID Personal Units 2014 (Alternative Purposes Only and Personal Units Perso

[1] Moderna ACIP Presentation 26-JUN-2024 (data shown for re-vaccination at 12-months post-dose 1), [2] Moderna ACIP Presentation 29-FEB-2024, [3] Icosavax Company Presentation 22-MAY-2023 (data shown for 225µg group), [4] Icosavax Press Release 12-DEC-2023. [5] Moderna ACIP Presentation 29-FEB-2024,

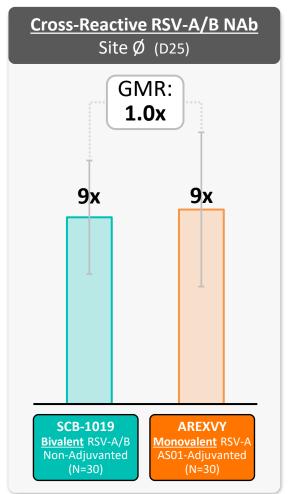


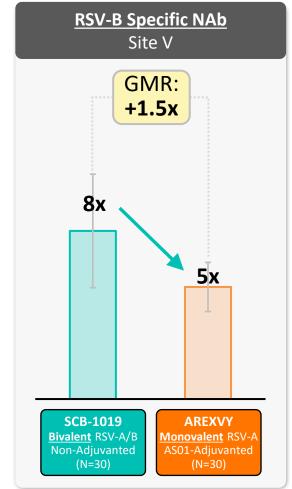
Potential for Bivalent SCB-1019 (RSV-A/B) to Induce Differentiated Immunological Breadth

Significant Differences Between Key RSV-A vs RSV-B NAb Epitopes

- >15 Amino Acid Differences within the Most Critical PreF-Specific Neutralization Sites Alone (Site Ø and Site V) (1)
- Bivalent SCB-1019 Induces Potentially Differentiated Immunological Breadth & "Quality of Neutralization"
 - Total RSV-A/B neutralization titers following vaccination may be influenced by high levels of NAbs induced against less potent neutralization sites which are not PreF-specific (e.g. Sites IV, III, II, I)
 - Phase 1 Exploratory Results: Bivalent RSV-A/B SCB-1019 induced a ~1.5x Higher Trend in Antibodies to an RSV-B Specific Neutralization Epitope compared to AREXVY (monovalent RSV-A), demonstrating potential for bivalent SCB-1019 to induced differentiated immunological breadth
 - Potential for SCB-1019 to induce greater & more sustained immunological breadth upon re-vaccination, by repeated recall & stimulation of RSV-B NAb epitope-specific memory B-cells, pending confirmation in subsequent clinical studies

PreF-Specific Neutralizing Antibody (NAb)-Competitive ELISA (GMFR)





Note: Bars represent GMFRs for Day 28 versus Day 0 (± standard error). Preliminary results shown for exploratory ELISA assays. Abbreviations: GMFR (Geometric Mean Fold Rise), GMR (Geometric Mean Ratio), NAb (Neutralizing Antibody). (1) Sacconnay et al., Sci. Transl. Med., 2023 (DOI: 10.1126/scitranslmed.adg6050).

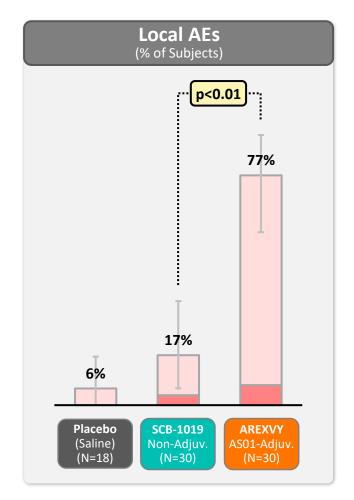


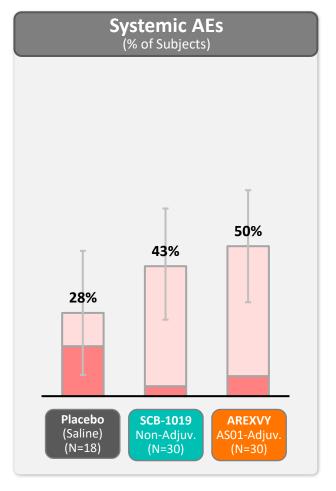
Clover SCB-1019 Phase 1: Safety & Reactogenicity Results

Safety & Reactogenicity Results

- Significantly Lower Rates of Local AEs Observed for Clover's non-adjuvanted SCB-1019 (16.7%)

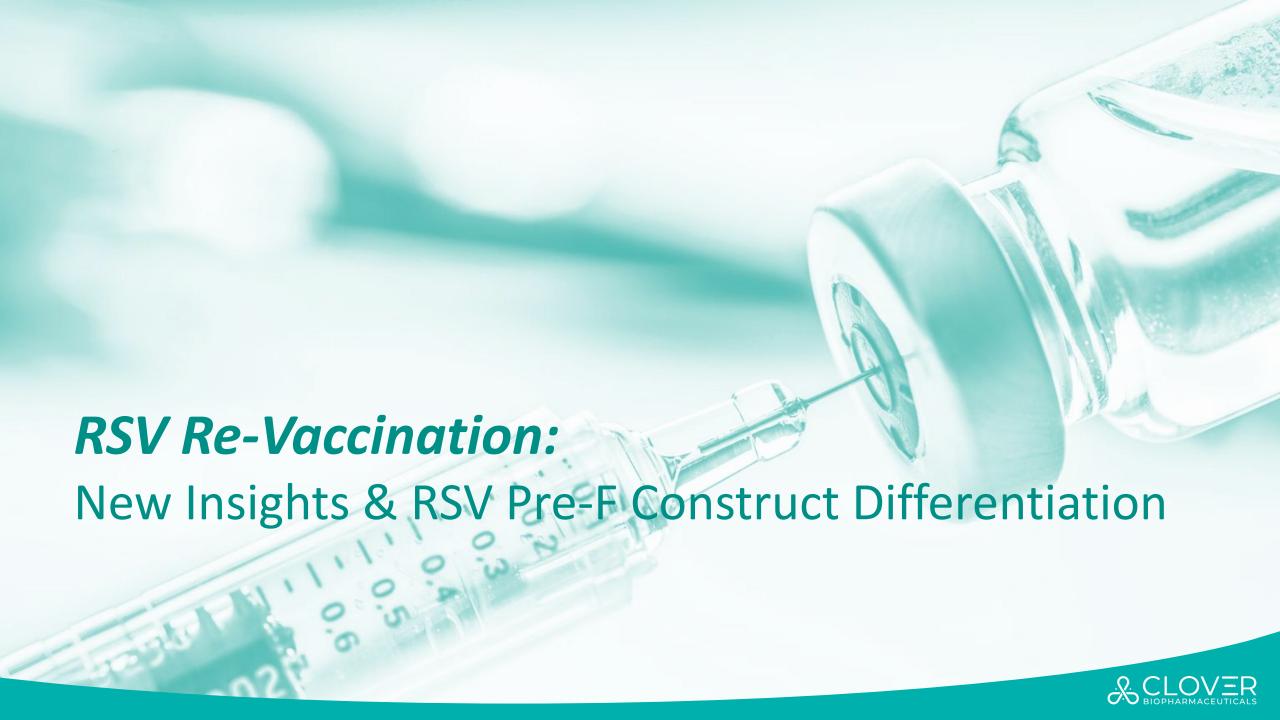
 Versus GSK's AS01-adjuvanted AREXVY (76.7%)
- ✓ SCB-1019 Local and Systemic AEs were Generally Mild for SCB-1019 and were Comparable to Saline Placebo
- ✓ No Vaccine Related Serious Adverse Events (SAEs), Adverse Events of Special Interest (AESIs), or AEs Leading to Discontinuation Observed
- **☑** Potential <u>Best-in-Class</u> Tolerability Profile









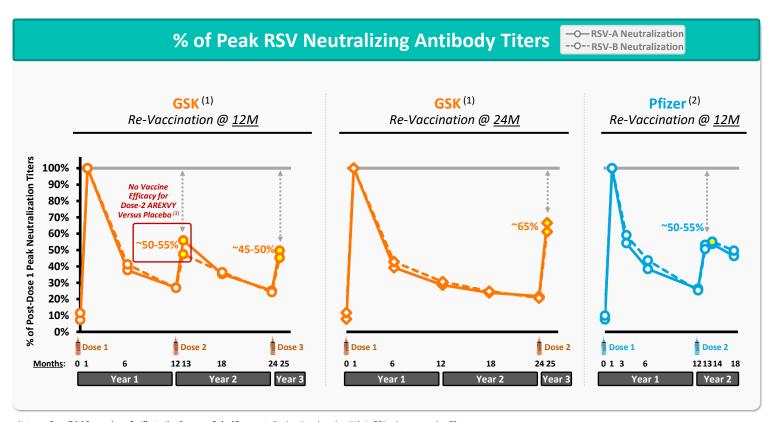


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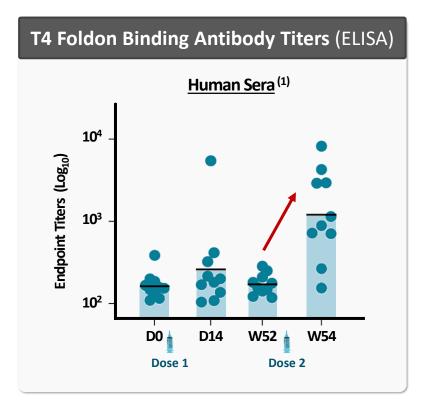


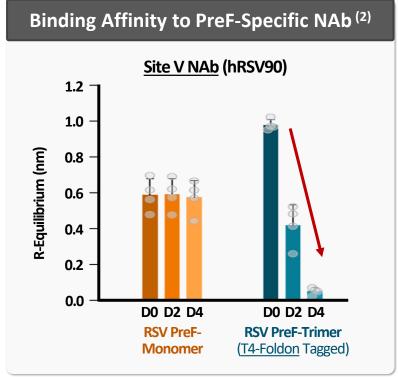
T4-Foldon Induces 'Off-Target' Immunes Responses in Humans & De-Stabilizes RSV PreF

Publication in Nature Microbiology (Dec 2024)

- <u>T4-Foldon Tagged RSV PreF Vaccines</u> Induce <u>'Off-Target' Immunes Responses in Humans</u>, NHPs & Mice
- T4-Foldon De-Stabilizes RSV PreF, Causing Loss of Binding to PreF-Specific NAbs







Source: DOI: 10.1038/s41564-024-01860-1.

- (1) Human participants (n=10) were immunized with JNJ's T4 foldon-tagged preF protein combined with Ad26-preF at week 0 and at week 52.
- (2) Biolayer interferometry assay. Samples stored at 4°C at Days 0, 2, 4.



RSV PreF Stabilization Strategies & Clover's Differentiated Approach

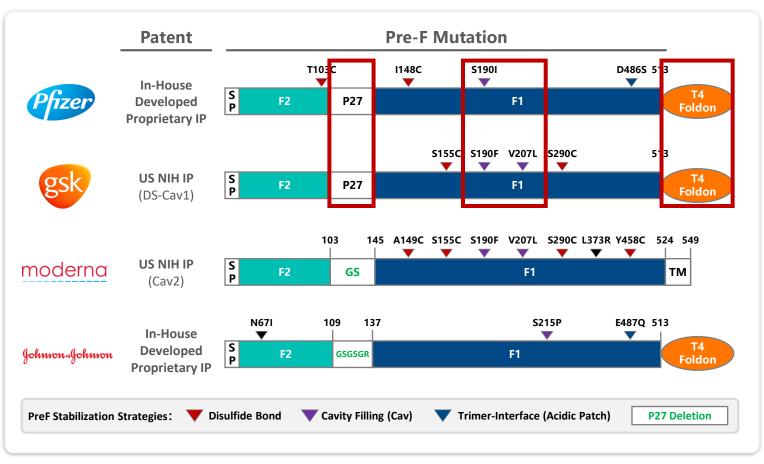
☑ SCB-1019: In-house Proprietary RSV PreF-Stabilizing Mutations + Trimer-Tag Platform

Clover's SCB-1019 Utilizes a Differentiated Approach to Producing & Stabilizing RSV PreF-Trimer

In-house Developed Proprietary Stabilizing Mutations:
Differentiated mutation approach compared to other companies and National Institute of Health (NIH);
Clover focused on minimizing number of mutations in a single region to preserve native-like Pre-F structure



Trimer-Tag: Trimer-Tag (derived from human procollagen) forms a flexible structure, enabling preservation of native-like trimeric Pre-F structure; potentially superior to T4 Foldon approach (utilized by GSK and Pfizer)

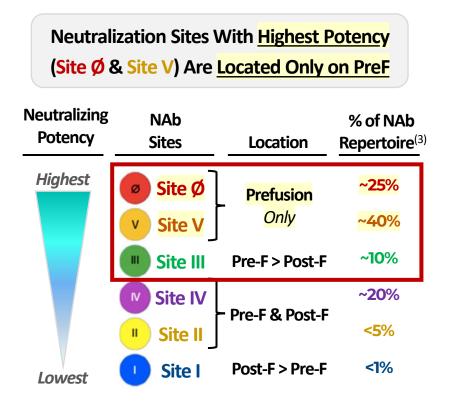


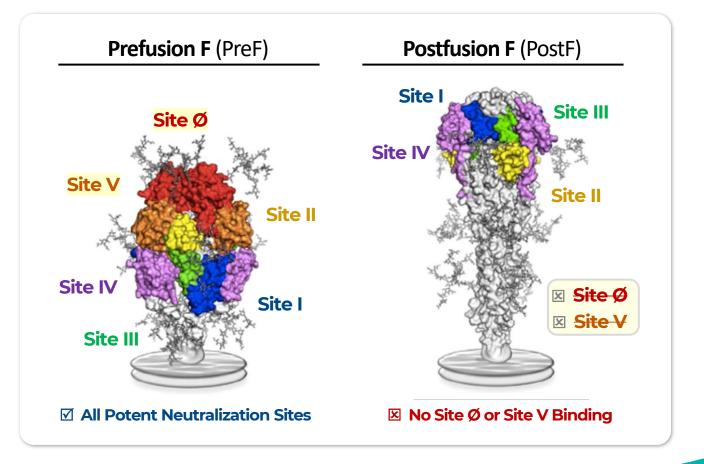
Note: Based on publicly-available information for reference-only.



Sites Ø, V, III Comprise ~75% of RSV NAb Repertoire & Are PreF-Specific/Preferred

- Only the Pref Conformation contains the most potent RSV neutralization sites (Site Ø, Site V, Site III) which may comprise ~75% of the overall NAb repertoire (3), whereas PostF does not (1)
- Stabilized PreF vaccines have demonstrated vaccine efficacy (GSK, Pfizer, Moderna), whereas PostF failed in previous clinical trials (2)





Note: NAb (Neutralizing Antibody).



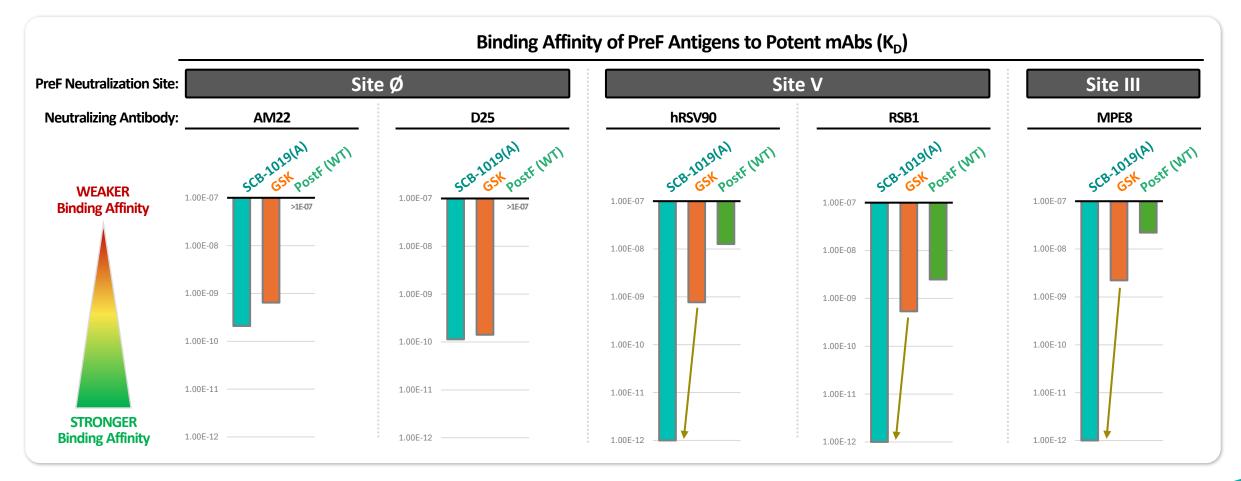
¹⁾ Taleb et al., Eur J Clin Microbiol Infect Dis., 2018 (<u>DOI</u>: 10.1007/s10096-018-3289-4).

⁽²⁾ Besteman & Bont, Am J Respir Crit Care Me, 2019 (DOI: 10.1164/rccm.201901-0233ED).

Gilman et al., Sci Immunol., 2016 (DOI: 10.1126/sciimmunol.aaj1879). Estimated percentage of high potency (0.05 μg/mL)) neutralizing antibody repertoire.

SCB-1019 Exhibits Differentiated & Stronger Binding Affinity to Site V and Site III NAbs

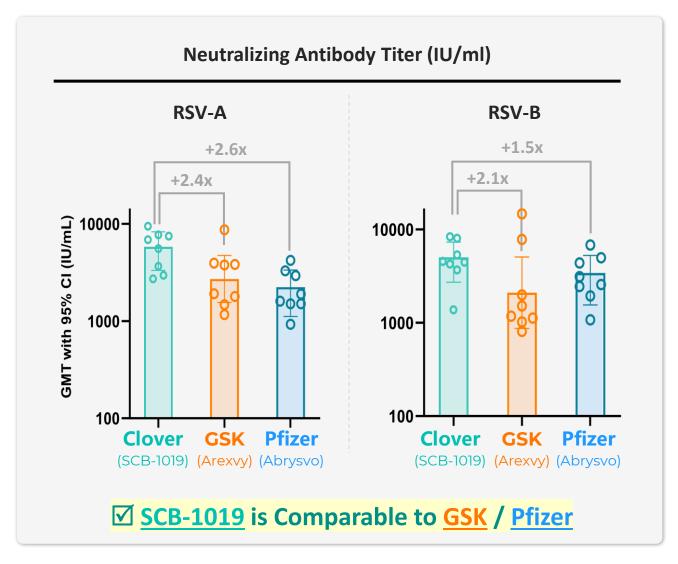
- Clover's RSV PreF Demonstrates Differentiated and Higher Binding Affinity than GSK (AREXVY) Against mAbs at Highly Potent Neutralization Sites (V, III)
- Results Could Potentially Indicate Clover's RSV PreF is More 'Native-Like' than GSK (AREXVY) & similar constructs (i.e. Pfizer)

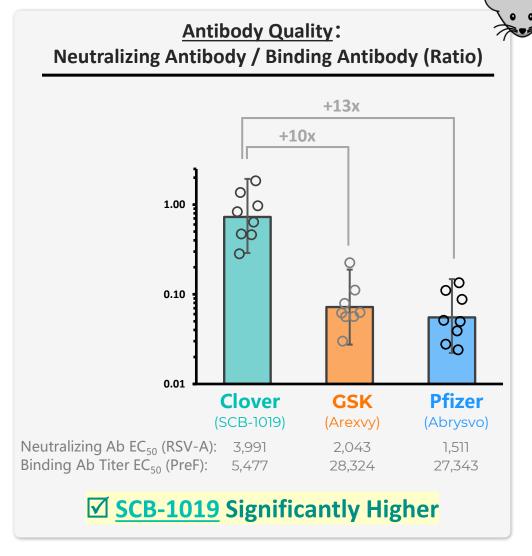


Note: Clover preclinical studies. K_D (Dissociation Constant) measured by ForteBio assay.



SCB-1019 Induces Differentiated 'Antibody Quality' in Mice





Note: Clover preclinical studies. Head-to-head comparison of SCB-1019 versus commercially-procured Arexvy (GSK) and Abrysvo (Pfizer) in primed mouse model. Mice were primed with live RSV-A virus, and after approximately 3 months, mice were given a single dose of vaccine (Day 0). Sera were collected on Day 14 (14 days post-vaccination) for neutralizing and binding antibody testing. SCB-1019 (0.36µg), Arexvy and Abrysvo were administered at equimolar doses. Geometric mean titers (GMT) ± 95% confidence intervals (95% CI) shown for antibody titers.



Phase 1: SCB-1019 Induces Differentiated 'Antibody Quality' in Humans Compared to GSK (AREXVY)

- Phase 1 Results: Group-level (n=30/group) trends observed for SCB-1019 inducing potentially higher ratios of functional antibodies (Total & Site-Specific NAb) to total binding antibodies (ELISA) compared to GSK (AREXVY)
 - SCB-1019: No significant changes in ratios at Day 28 compared to baseline (Day 0), suggesting preservation of antibody repertoire induced by prior natural RSV infections (i.e. SCB-1019 PreF is native-like)
 - AREXVY: Statistically significant <u>decreases</u> in ratios of <u>NAb/Binding Ab</u> (GMFR 0.66x) & <u>Site V/Binding Ab</u> (GMFR 0.49x) observed at Day 28, suggesting induction of non-neutralizing and/or 'off-target' antibodies
- If SCB-1019 is indeed a more 'native-like' PreF, then
 potentially greater differentiation could be
 observed in a heterologous re-vaccination setting
 (i.e. using SCB-1019 to re-vaccinate people
 previously receiving an initial dose of AREXVY)
- If confirmed in subsequent clinical studies, results could potentially confirm that <u>Clover's Trimer-</u> <u>Tagged & stabilized PreF is superior to</u> <u>GSK/Pfizer's T4-Foldon Tagged PreF Constructs</u>



Abbreviations: GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise based on Day 28/Day 0), NAb (Neutralizing Antibody). Note: Dots represent GMTs (\pm 95% confidence intervals). Total binding antibody results based on RSV PreF binding ELISA assay (EC_{50}). Total neutralizing antibody results based on RSV-A neutralization assay (IU/mL). Site Ø NAb and Site V NAb results based on competitive ELISA assays (IC_{50}). Preliminary results shown for validated RSV neutralizing antibody assay and exploratory ELISA assays.



Summary of RSV Re-Vaccination Data & Clover's Potential Differentiation

GSK/Pfizer's Re-Vaccination
Results at 1- and 2-Year
Intervals Have been
Unsuccessful to-Date

- Both GSK/Pfizer's RSV Pref utilize T4-Foldon Trimerization Tag + Cavity Filling Mutations (with p27 preserved)
- T4-Foldon (bacteriophage derived) reported to induce 'off-target' immune responses in humans and may destabilize Pref (1)

<u>Clover's SCB-1019</u> Preclinical & Clinical Results To-Date

Demonstrate a <u>Differentiated</u>

RSV PreF Construct

Clover's Trimer-Tagged RSV PreF (SCB-1019) is Differentiated & Potentially More 'Native-Like' than GSK & Pfizer

- In Vitro mAb Binding: Differentiated & higher binding affinity than GSK (AREXVY) against mAbs at highly potent PreF NAb sites (V, III)
- Mouse NAb-to-Binding Antibody Ratio: Significantly higher ratios of NAb-to-Binding Antibodies observed for SCB-1019 versus GSK/Pfizer
- Phase 1 NAb-to-Binding Antibody Ratios: Higher trends observed for SCB-1019 versus GSK in Phase 1 in vaccine-naïve older adults
- <u>Trimer-Tag is Immuno-Silent in Humans</u>: Dosed in >15,000 subjects with Trimer-Tagged COVID-19 vaccine SCB-2019 (CpG 1018/alum), with no humoral or cellular anti-Trimer-Tag responses observed

Working Hypothesis for GSK/Pfizer's Re-Vaccination Challenges & Clover's Planned Next Steps

- GSK/Pfizer's T4-foldon tagged RSV PreF constructs may be non-native and/or unstable in vivo, exposing non-native, non-neutralizing antibody epitopes on RSV PreF (as well as off-target T4-foldon epitopes), which are immunologically primed by Dose 1
- Upon <u>Re-vaccination (Dose 2)</u> of GSK/Pfizer, <u>antibody responses against non-native epitopes</u> (primed by Dose 1) and/or <u>undesired</u>
 <u>'negative' affinity maturation (against altered NAb epitopes)</u> could <u>interfere with desired induction of potent PreF NAbs</u> (especially if non-native epitopes are immuno-dominant)
- Potential to overcome GSK/Pfizer's current re-vaccination challenges utilizing a heterologous re-vaccination (Dose 2) with Clover's differentiated & potentially more 'native-like' Trimer-Tagged RSV PreF vaccine candidate SCB-1019
- To be further evaluated in Clover's Re-Vaccination Clinical Trial for SCB-1019 (Head-to-Head vs AREXVY) Planned to Initiate in 2025

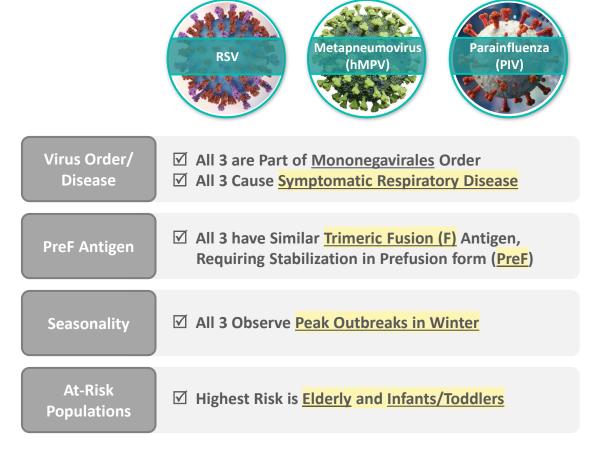


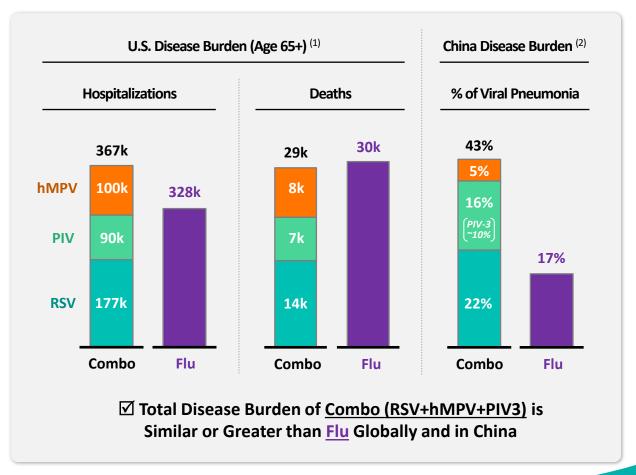
RSV Combination Vaccine Development (RSV + hMPV ± PIV3)



Potential for Respiratory Combo Vaccine (RSV + hMPV + PIV3) LCM Opportunity

- Total Disease Burden of Combo (RSV+hMPV+PIV) is similar or greater than Flu Globally and in China; combination vaccine is a compelling opportunity & unmet need
- <u>Directly leveraging Clover's RSV experience</u> to develop '<u>Respiratory Combo Vaccines</u>' across mononegavirales order of viruses (<u>RSV + hMPV ± PIV3</u>)
- <u>Trimer-Tag protein subunit</u> has <u>platform advantages</u> for combo versus <u>mRNA</u> (combo dose is limited by safety) and <u>VLPs</u> (complicated CMC)





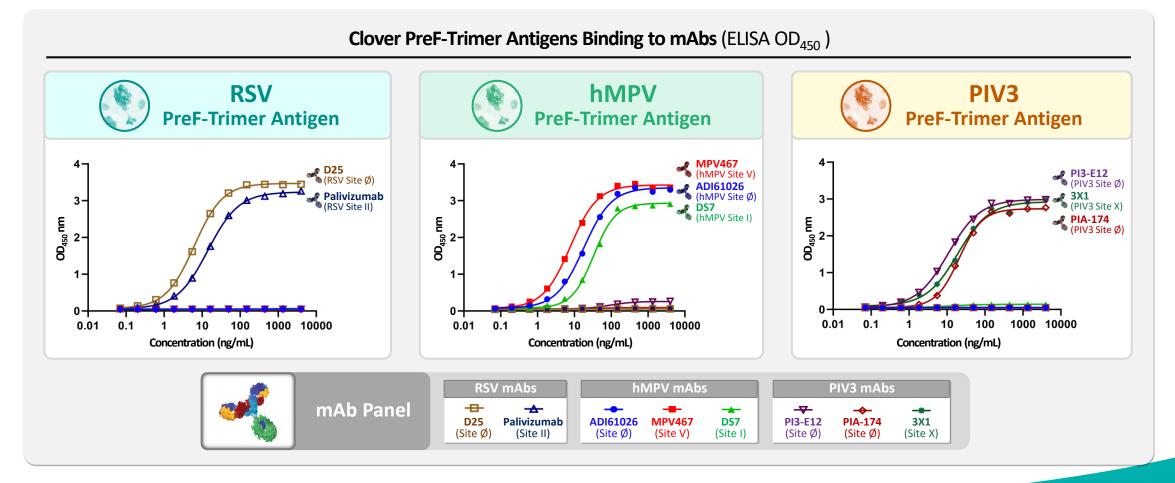
¹⁾ Sources: [A] Widmer et al., 2012; [B] Russell et al., 2019 (62% of RSV); [C] Colosia et al., 2017; [D] Using RSV rate from Colosia 2017 as proxi. [E] https://www.cdc.gov/rsv/research/us-surveillance.html [F] Compilated data from CDC, 9 seasons from 2010-2011 to 2018-2019 https://www.cdc.gov/flu/about/burden/index.html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

SCB-1019 is being Utilized to Develop RSV Respiratory Combination Vaccine Candidates

- ☑ Clover's PreF-Trimers (RSV, hMPV, PIV3) Bind Potently to Homologous PreF-Specific mAbs for Critical Neutralization Epitopes (Ø, V, X)
- ☑ Confirmed Stabilized Prefusion (PreF) Conformations
- ✓ No Immune Interference Observed in Preclinical In Vivo Immunogenicity Studies To-Date





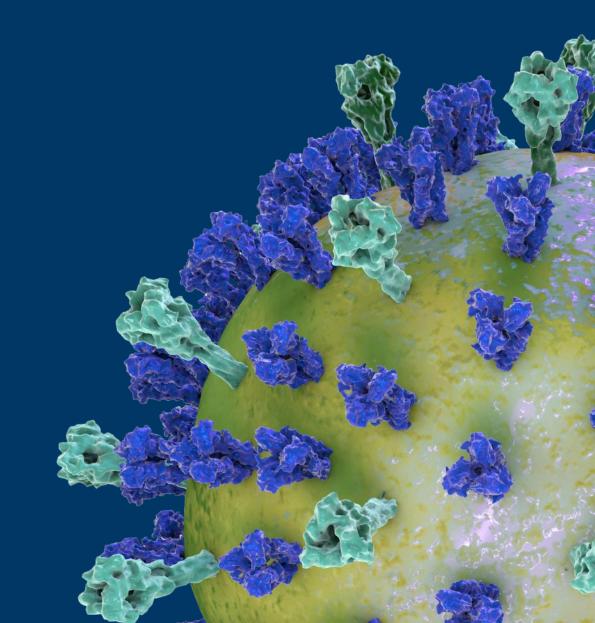
Clover's Planned Next Steps

☑ OCT-2024: Head-to-Head Clinical Results Versus GSK (AREXVY) De-Risks & Indicate Clover's Potential Best-in-Class Combined Efficacy & Safety Profile for SCB-1019 (Non-Adjuvanted Bivalent RSV-A/B Vaccine Candidate) **☑** Q4-2024: ☑ <u>DEC-2024</u>: Preclinical & Clinical Data Supporting that Clover's Trimer-Tagged RSV PreF (SCB-1019) is Differentiated & Potentially More 'Native-Like' than GSK & Pfizer ☐ To Initiate Clinical Trial Evaluating SCB-1019 in an RSV Re-Vaccination Setting **Planned** 2025: ☐ To Initiate Clinical Trial for RSV Respiratory Combination Vaccine (RSV + hMPV ± PIV3)





Appendix



Surface antigens of many viruses & pathogens are <u>naturally-trimeric in structure</u>; Key objective of vaccine development is to preserve the antigen's <u>native structure</u>





Epstein-Barr (EBV)

gB antigen

Rotavirus

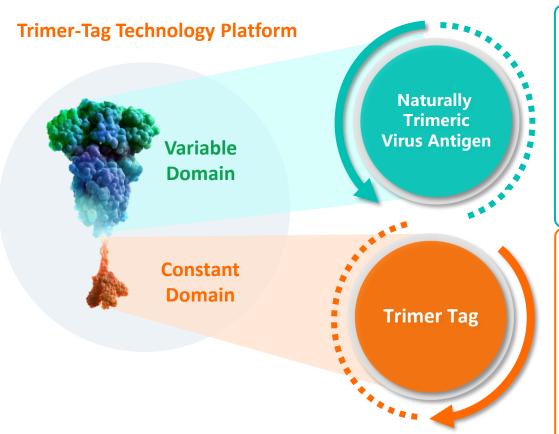
VP8 antigen

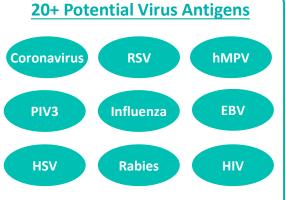
HIV

Gp120/41 antigen

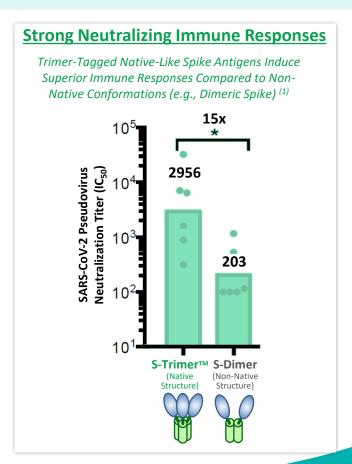
Clover's Trimer-Tag Technology Platform for Vaccine Development

- 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" lneutralizing responses); does not induce ADA/pre-existing immunity issue (enables repeated boosting & positive safety profile)
- Validated technology: Platform has been fully validated by COVID-19 vaccine (SCB-2019) that is authorized for Emergency Use in China





- ✓ 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; affinitypurification achieves high antigen purity



Note: Representative list of viruses with naturally trimeric spike antigens is illustrative and not exhaustive. Abbreviation: ADA (Anti-Drug Antibodies).



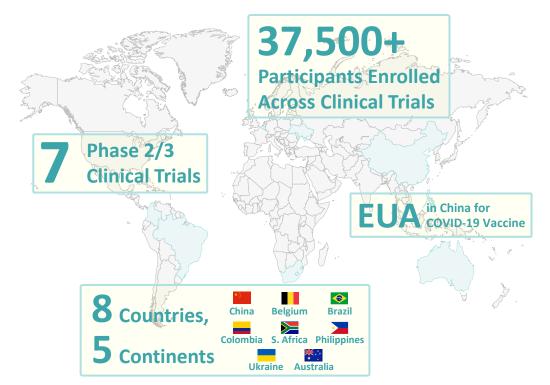
^{*} A "trimer" refers to a molecule or an anion formed by combination or association of three molecules or ions of the same substance. Trimerization is a chemical reaction that uses three identical molecules to produce a single trimer. Proteins that are created through the joining of two or more genes 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 refers to a protein that 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 5-Trimer (Trimer-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



- **☑** 37,500+ Participants Enrolled Across Trials in 8 Countries
- 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 C P I to Support
 Clover Establishing its Vaccine Platform (Trimer-Tag Platform + Vaccine Manufacturing Capabilities)























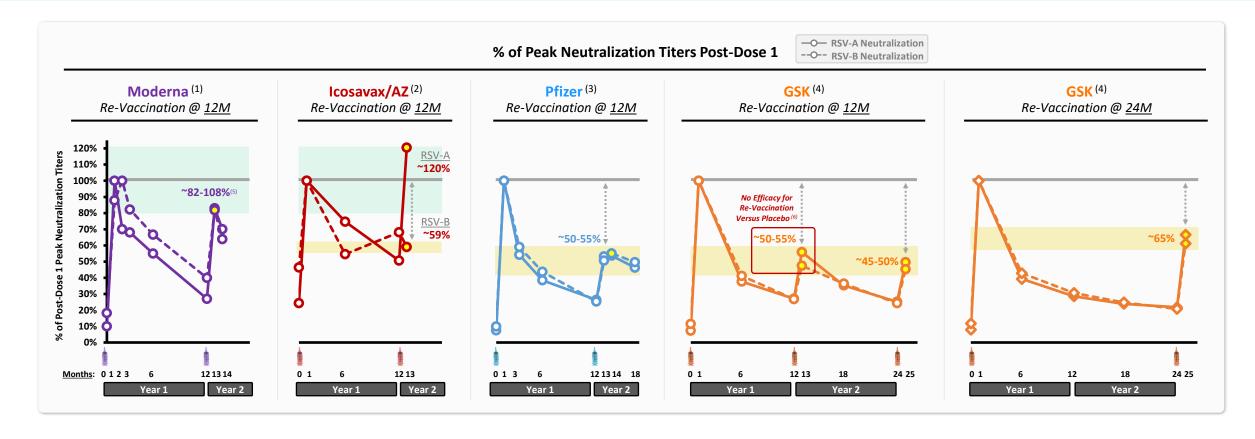


☑ Trimer-Tag Platform Published in the Most Renowned Scientific Journals Globally (Lancet, Nature Communications, JID, etc.)



Re-Vaccination Issues Encountered for GSK & Pfizer RSV Vaccines

- GSK/Pfizer: Neutralization Titers Only Reach <u>~45-65% of Peak Levels</u> Following Re-Vaccination, Potentially Due to Immune-Interference from T4-Foldon Trimerization Tag Utilized by Both Vaccines
- GSK/Pfizer Announced they are now Evaluating Re-Vaccination at 3- and 5-Year Intervals in Phase 3 Studies, but Efficacy Durability Requires Re-Vaccination at ~2-Year Intervals
- Clover's Trimer-Tag Platform (Immuno-Silent in Humans) May be able to Overcome GSK/Pfizer's Re-Vaccination Issue
- Moderna/Icosavax: Data Demonstrate that RSV Neutralization is Boostable, but Moderna mRNA Efficacy Durability is Inferior (<1 Year) & Icosavax Fails to Boost RSV-B Neutralization



Significant Market Opportunity Exists for <u>Differentiated RSV Vaccines</u> that can <u>Effectively Re-Vaccinate with Good Durability/Breadth</u>



Note: Cross Trial Comparisons for Illustrative Purposes Only. Moderna, Icosavax and Pfizer neutralization titers based on IU/mL. GSK units expressed as ED₆₀.

Sources: (1) Moderna ACIP Presentation (29-FEB-2024), (2) Icosavax Company Presentation IVX-121 (28-JUN-2023), (3) Pfizer 2023 VRBPAC Company Briefing Document, (4) GSK ACIP Presentation (26-JUN-2024).

⁽⁵⁾ Moderna reported additional re-vaccination immunogenicity data at 26-JUN-2024 ACIP meeting in adults aged ≥50 years, demonstrating geometric mean ratios (GMR) of re-vaccination versus first dose neutralization titers of 1.08 (95% CI: 0.99 – 1.17) for RSV-A and 0.91 (95% CI: 0.84 – 0.99) for RSV-B. meeting non-inferiority criteria (LB of 95% CI of GMRs >0.667).

^{(6) 21} JUNE 2023 ACIP Meeting (GSK Presentation). Based on primary efficacy endpoint (RSV-LRT≥2 Symptoms/Signs).

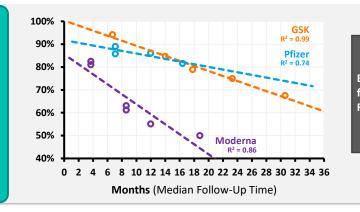
Durability of RSV Vaccine Efficacy from Phase 3 Clinical Trials

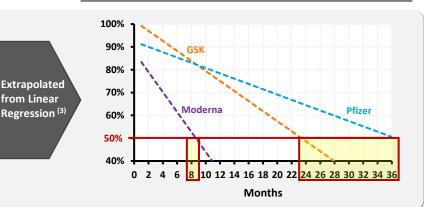
- mRNA (Moderna) Efficacy Durability Trend Appears Inferior Versus Protein-Based RSV Vaccines, with Efficacy Lasting <1 Year (Even Against 'Severe' forms of RSV Disease)
- Re-Vaccination for all RSV Vaccines is Needed (Similar to Flu & COVID-19), Potentially Every 2 Years for Protein-Based RSV Vaccines (GSK/Pfizer)

Cumulative Efficacy @ Median Follow-Up Time (Dotted Lines Represent Linear Regression (3,4))

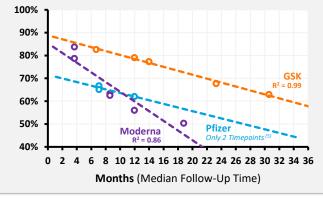
Monthly Efficacy Point Estimates (Extrapolated from Linear Regression^(3,4))

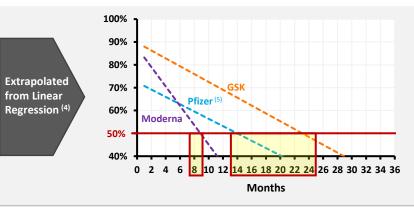
Vaccine Efficacy Against 'Severe' Forms of RSV Disease (1)





Vaccine Efficacy Against 'Moderate-to-Severe' Forms of RSV Disease (2) (Note: Phase 3 Primary Endpoints)





☑ Efficacy for Protein-**Based RSV Vaccines Appears Durable and** Superior to mRNA, with **Potential Re-Vaccination** Interval of ~2 Years

Note: Cross Trial Comparisons for Illustrative Purposes Only (Efficacy endpoints are different across vaccines and studies

Sources: ACIP Meetings including 21 JUNE 2023 (GSK and Pfizer Presentations), 29 FEB 2024 (Moderna Presentation), 26 JUNE 2024 (GSK, Pfizer, Moderna and CDC Presentations). 28 FEB 2023 FDA VRBPAC Meeting (Pfizer Presentations). 08 OCT 2024 GSK Press Release GSK (RSV-LRTD >2 Signs or 'Severe' Assessment by PI). Pfizer (RSV-LRTD >3 Symptoms/Signs). Moderna (RSV-LRTD >3 Symptoms)

GSK (RSV-LRTD ≥2 Symptoms/Signs for ≥24 Hours), Pfizer (RSV-LRTI ≥2 Symptoms/Signs), Moderna (RSV-LRTD ≥2 Symptoms).



Elderly RSV Vaccine Phase 3 Efficacy Durability: Summary Reference Data

Vaccine Efficacy Against <u>'Severe' RSV Disease</u> (1)

	GSK (AREXVY) RSV-LRTD ≥2 Signs or 'Severe' Assessment by PI						Pfizer (ABRYSVO) RSV-LRTI ≥3 Symptoms/Signs					Moderna (MRESVIA) RSV-LRTD ≥3 Symptoms						
Phase 3 Median Follow-Up Time:	-	12.0 Months	14.0 Months	17.8 Months	23.3 Months	30.6 Months	7.1 Months		12.0 Months	13.9 Months	16.4 Months	3.7 Months		8.6 Months		12.0 Months	18.8 Months	
Vaccine Efficacy (95% CI)	94.1% (62.4 – 99.9)		84.6% (56.4 – 96.1)	78.8% (52.6 – 92.0)	74.9% (48.4 – 89.2)	67.4% (42.4 – 82.7)	85.7% (32.0 - 98.7)	88.9% ()	86.0% (63.0 - 96.0)	~84% ⁽³⁾ ()	81.5% (48.2 - 80.0)	82.4% (34.8 - 95.3)	80.9% (50.1 - 92.7)	63.0% (37.3 - 78.2)	61.1% (34.7 - 76.8)	55.0% (31.0 - 71.0)	49.9% (27.8 - 65.6)	
Cases: Vaccine	1 (12,466 Subj.)		4 (12,469 Subj.)	7 (12,469 Subj.)	9 (12,468 Subj.)	15 (12,468 Subj.)	2 (16,466 Subj.)	2 (~18,000 Subj.)		5 (~10,000 Subj.)	10 ()	3 (17,572 Subj.)	5 (17,561 Subj.)	19 (18,112 Subj.)	20 (18,074 Subj.)		46 (18,181 Subj.)	
Cases: Placebo	17 (12,494 Subj.)		33 (12,498 Subj.)	48 (12,498 Subj.)	54 (12,498 Subj.)	75 (12,498 Subj.)	14 (16,308 Subj.)	18 (~18,000 Subj.)		32 (~10,000 Subj.)	54 ()	17 (17,516 Subj.)	26 (17,503 Subj.)	51 (18,045 Subj.)	51 (18,010 Subj)		91 (18,132 Subj.)	
Reference	ACIP Meeting 21 JUNE 2023 (GSK Presentation)		ACIP Meeting 21 JUNE 2023 (GSK Presentation)	ACIP Meeting 21 JUNE 2023 (GSK Presentation)	ACIP Meeting 26 JUNE 2024 (GSK Presentation)	GSK Press Release 08 OCT 2024	VRBPAC Meeting 28 FEB 2023 (Pfizer Present.)	ACIP Meeting 21 JUNE 2023 (Pfizer Present.)	ACIP Meeting 26 JUNE 2024 (CDC Presentation)	ACIP Meeting 21 JUNE 2023 (Pfizer Present.)	ACIP Meeting 26 JUNE 2024 (Pfizer Present.)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	ACIP Meeting 29 FEB 2024 (Moderna Present)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	ACIP Meeting 26 JUNE 2024 (CDC Presentation)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	

Vaccine Efficacy Against 'Moderate-to-Severe' RSV Disease (2)

	GSK (AREXVY) RSV-LRTD ≥2 Symptoms/Signs for ≥24 Hours						Pfizer (ABRYSVO) RSV-LRTI ≥2 Symptoms/Signs					Moderna (MRESVIA) RSV-LRTD ≥2 Symptoms						
Phase 3 Median Follow-Up Time:	6.7 Months	12.0 Months	14.0 Months	17.8 Months	23.3 Months	30.6 Months	7.1 Months		12.0 Months	13.9 Months	16.4 Months	3.7 Months		8.6 Months		12.0 Months	18.8 Months	
Vaccine Efficacy (95% CI)	82.6% (57.9 - 94.1)	79.0% (58.0 - 90.0)	77.3% (60.2 - 89.0)	67.2% (48.2 - 80.0)	67.7% (52.3 - 78.7)	62.9% (46.7 – 74.8)	66.7% (28.8 - 85.8)	65.1% ()	62.0% (41.0 - 76.0)	~63% ⁽³⁾ ()		83.7% (66.0 - 92.2)	78.7% (62.8 - 87.9)	63.3% (48.7 - 73.7)	62.5% (47.7 - 73.1)	56.0% (42.0 - 67.0)	50.3% (37.5 - 60.7)	
Cases: Vaccine	7 (12,466 Subj.)		15 (12,469 Subj.)	30 (12,469 Subj.)	32 (12,468 Subj.)	48 (12,468 Subj.)	11 (16,308 Subj.)	15 (~18,000 Subj)		38 (~10,000 Subj.)		9 (17,572 Subj.)	15 (17,561 Subj.)	47 (18,112 Subj.)	48 (18,074 Subj.)		113 (18,181 Subj.)	
Cases: Placebo	40 (12,494 Subj.)	-	85 (12,498 Subj.)	139 (12,498 Subj.)	154 (12,498 Subj.)	215 (12,498 Subj.)	33 (16,308 Subj.)	43 (~18,000 Subj)		88 (~10,000 Subj)		55 (17,516 Subj.)	70 (17,503 Subj.)	127 (18,045 Subj.)	127 (18,010 Subj)		225 (18,132 Subj.)	
Reference	ACIP Meeting 21 JUNE 2023 (GSK Presentation)	ACIP Meeting 26 JUNE 2024 (CDC Presentation)	ACIP Meeting 21 JUNE 2023 (GSK Presentation)	ACIP Meeting 21 JUNE 2023 (GSK Presentation)	ACIP Meeting 26 JUNE 2024 (GSK Presentation)	GSK Press Release 08 OCT 2024	VRBPAC Meeting 28 FEB 2023 (Pfizer Present.)	ACIP Meeting 21 JUNE 2023 (Pfizer Present.)	ACIP Meeting 26 JUNE 2024 (CDC Presentation)	ACIP Meeting 21 JUNE 2023 (Pfizer Present.)		ACIP Meeting 26 JUNE 2024 (Moderna Present)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	ACIP Meeting 29 FEB 2024 (Moderna Present)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	ACIP Meeting 26 JUNE 2024 (CDC Presentation)	ACIP Meeting 26 JUNE 2024 (Moderna Present)	

Note: Cross Trial Comparisons for Illustrative Purposes Only (Efficacy endpoints are different across vaccines and studies).

Sources: ACIP Meetings including 21 JUNE 2023 (GSK and Pfizer Presentations), 29 FEB 2024 (Moderna Presentation), 26 JUNE 2024 (GSK, Pfizer, Moderna and CDC Presentations), 28 FEB 2023 FDA VRBPAC Meeting (Pfizer Presentations), 29 FEB 2024 (Moderna Presentation), 26 JUNE 2024 (GSK, Pfizer, Moderna and CDC Presentations), 28 FEB 2023 FDA VRBPAC Meeting (Pfizer Presentations), 29 FEB 2024 (Moderna Presentations), 20 JUNE 2024 (GSK, Pfizer, Moderna Presentations),



^{(1) &}lt;u>Severe RSV Endpoints</u>: GSK (RSV-LRTD ≥2 Signs or 'Severe' Assessment by PI), Pfizer (RSV-LRTI ≥3 Symptoms/Signs), Moderna (RSV-LRTD ≥3 Symptoms).

⁽²⁾ Primary Endpoints: GSK (RSV-LRTD ≥2 Symptoms/Signs for ≥24 Hours), Pfizer (RSV-LRTI) ≥2 Symptoms/Signs), Moderna (RSV-LRTD ≥2 Symptoms).

Pfizer data for cumulative vaccine efficacy at 13.9 months median follow-up duration was not disclosed (only case splits for Season 1 and Season 2 respectively were disclosed, and cases collected in Season 2 were only in Northern Hemisphere representing approximately ~55% of evaluable subjects in Season 1 enrolled in the RENOIR Phase 3 study; cases collected for efficacy analysis in Season 1 also included Southern Hemisphere countries).



Thank You!

https://www.cloverbiopharma.com