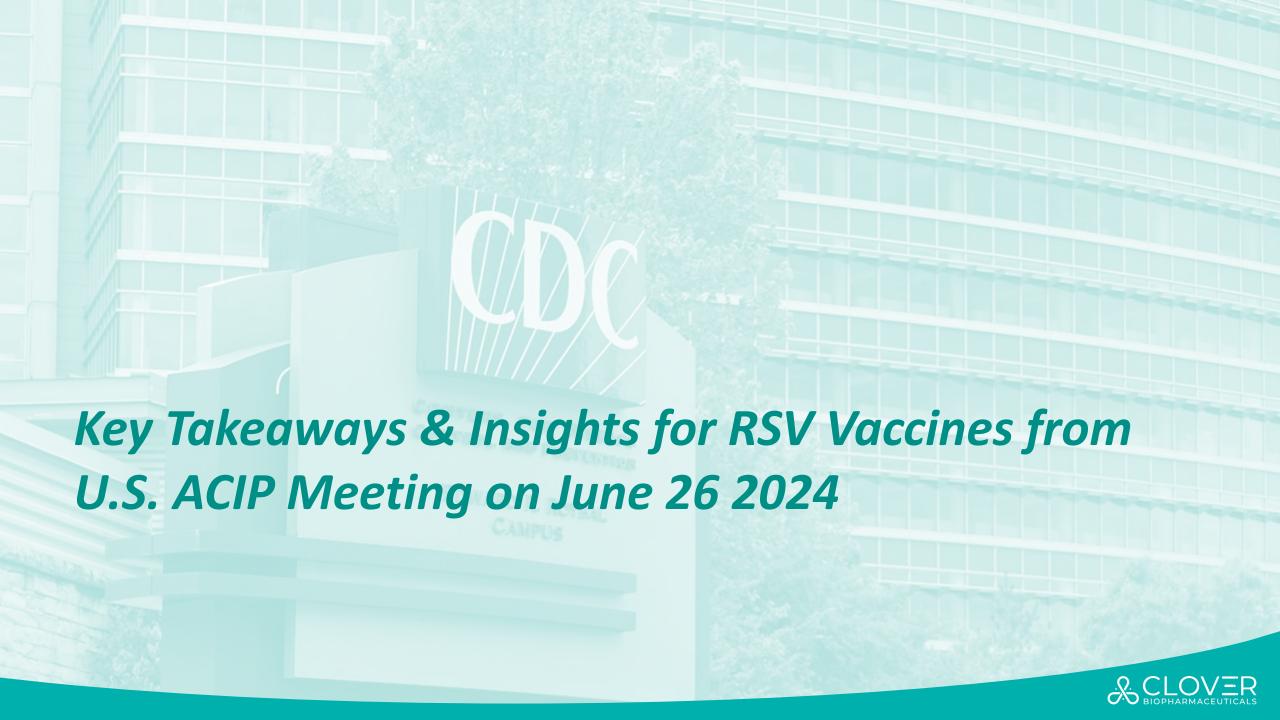




June-2024 ACIP Takeaways for RSV Vaccines & Clover SCB-1019 Phase 1 Data in Older Adults

July 2024



JUNE 26 2024 ACIP Meeting:

Key Summary Takeaways for RSV Vaccine Field

ACIP Recommendation for RSV Vaccines '24-25 Season

CDC Voted to Incrementally Expand Recommendation for RSV Vaccination in Upcoming 2024-2025 Season Compared to Previous Season (2023-2024)

<u>Adults ≥75 Years</u>: <u>Universal Recommendation</u> to Receive RSV Vaccine (Recommendation for 'Shared Clinical Decision Making' in 2023-2024)

✓ Adults 60 to 74 Years: Individuals with Increased Risk of Severe RSV Disease Should Receive RSV Vaccine

Key ACIP Updates

Implications for Field/Next Steps

Durability of Efficacy

- Moderna Durability of Efficacy is <1 Year, Even Against Severe Forms
 of RSV Disease (Similar to mRNA COVID-19 Vaccines)
- GSK & Pfizer Durability of Efficacy is ~2 Years, Indicating Re-Vaccination May be Needed at 2-Year Intervals (Prior to 3rd Season)



- ☑ Positive Differentiation for Protein-Based RSV Vaccines vs mRNA
- Upcoming Season (Fall/Winter 2024) to Observe Impact of <u>mRNA's</u>
 <u>Inferior Efficacy Durability on Market Share/Sales</u> (vs GSK/Pfizer)

Re-Vaccination

- Increased Spotlight on GSK & Pfizer Re-Vaccination Issues
- GSK Data Shows Re-Vaccination at 12- or 24-Month Intervals Cannot Boost RSV NAbs Back to Post-Dose 1 Levels (~45-65%)
- Moderna Re-Vaccination at 12-Months Can Successfully Boost RSV NAbs, but Efficacy Duration is <1 Season...</p>



- **GSK & Pfizer's Re-Vaccination Issues** Could Potentially be Caused by Immune Interference Induced by their <u>T4-Foldon</u> Trimerization Tag?
- Potential Opportunity & Differentiation for Clover (Trimer-Tag Technology is Immuno-Silent in Humans)
- Re-Vaccination is Majority of Long-Term Market Opportunity

GBS Risk

(Guillain-Barre Syndrome)

- FDA Concluded that Risk-Benefit for RSV Vaccines is Positive, and Increased Risk of GBS is Not Yet Conclusive (Trend of Increased GBS Risk is Observed, with Pfizer Trending Higher than GSK)
- However, Potential GBS Risk Played a Role in Limiting ACIP's Universal Vaccination Recommendation to Age 75+ Years (Recommendation for Age 60-74 Years Limited to At-Risk Individuals)



- Real-World Data in Year 2 of Launch (2024-2025 Season) Could Provide Robust Confirmatory Data & Insights (by FEB-2025 ACIP)
 - If Moderna also observes an increased GBS risk, could confirm GBS risk as a 'class effect' across RSV PreF vaccines



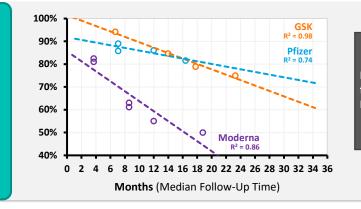
JUNE 26 2024 ACIP Meeting: Durability of Efficacy from Phase 3 Trials

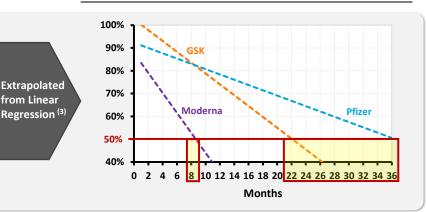
- mRNA (Moderna) Efficacy Durability Trend Appears Inferior Versus Protein-Based RSV Vaccines, with Efficacy Lasting <1 Year (Even Against 'Severe' forms of RSV Disease)
- Re-Vaccination for all RSV Vaccines is Needed (Similar to Flu & COVID-19), Potentially Every ~2 Years for Protein-Based RSV Vaccines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

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

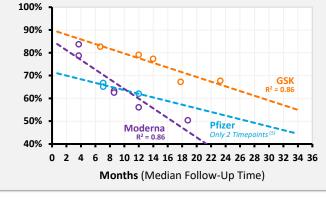
Monthly Efficacy Point Estimates (Extrapolated from Linear Regression^(3,4))

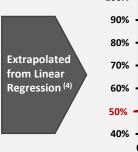
Vaccine Efficacy Against 'Severe' Forms of RSV Disease (1)

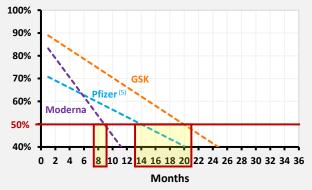




Vaccine Efficacy Against 'Moderate-to-Severe' Forms of RSV Disease (2) (Note: Phase 3 Primary Endpoints)







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

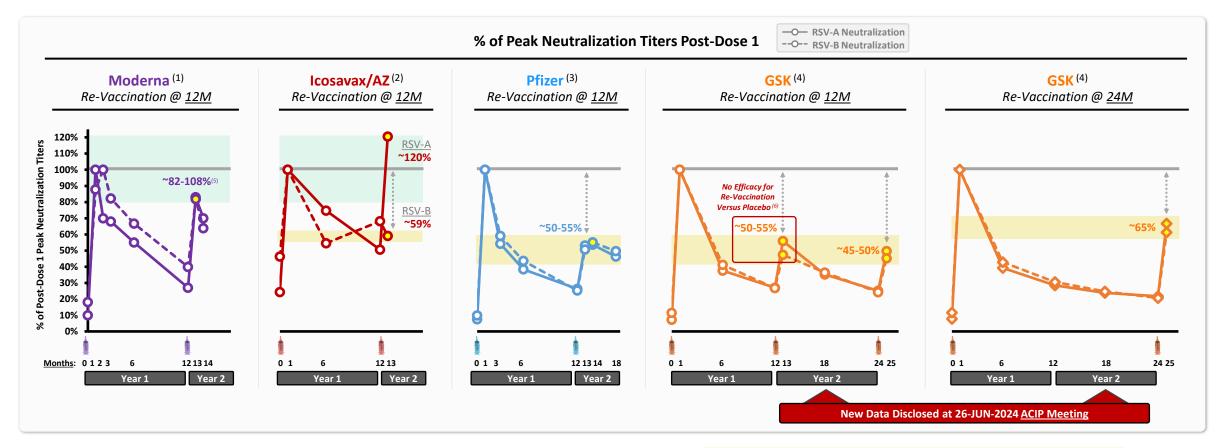
Severe RSV Endpoints: Primary Endpoints

GSK (Y = -0.0103x + 0.8997) | Pfizer (Y = -0.008x + 0.7155) | Moderna (Y = -0.0212x + 0.8535)



JUNE 26 2024 ACIP Meeting: Re-Vaccination Issue for GSK & Pfizer Further Highlighted

- GSK/Pfizer: Neutralization Titers Only Reach ~45-65% of Peak Levels 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 4-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 Differentiated RSV Vaccines that can Effectively Re-Vaccinate with Good Durability/Breadth



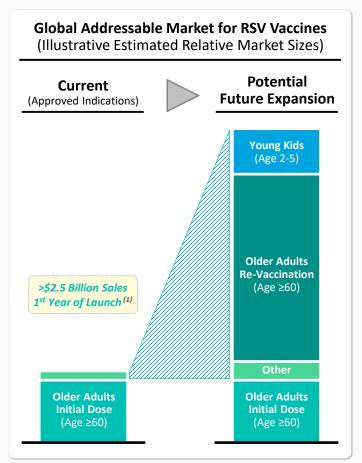
Cross Trial Comparisons for Illustrative Purposes Only. Moderna, Icosayax and Pfizer neutralization titers based on IU/mL, GSK units expressed as EDec Sources: (1) Moderna ACIP Presentation (29-FEB-2024), (2) Icosavax Company Presentation IVX-121 (28-JUN-2023), (3) Pfizer 2023 VRBPAC Company Briefing Document, (4) GSK ACIP Presentation (26-JUN-2024).

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).

Global RSV Vaccine Market Views: Significant Expansion & LCM Opportunities

- Significant Untapped Market Expansion Opportunities (Older Adult Re-Vaccination, Young Kids), Requiring Platform/Product Differentiation
- Longer-Term Lifecycle Management Opportunities (Respiratory Combination Vaccines) to Continue Driving Market Share & Value



Considerations & Market Dynamics for Each Indication



Young Kids (Age 2-5)

- Higher Disease-Burden for RSV in Young Kids Versus Older Adults Based on Epi Data
- Less Competition Expected: Novel Adjuvant (GSK) Safety Concerns & mRNA Inferior Tolerability Profile May Limit Development Scope & Market Uptake in Young Kids
- Untapped Opportunity: Field is in Early-to-Mid Stage (Pfizer Ph1 / Moderna Ph2)



Older Adults **Re-Vaccination** (Age ≥60)

- Largest Addressable Market: Re-vaccination to Drive Recurrent Sales from Each Vaccinee in Large Elderly Population Pool Globally (Similar to Seasonal Flu Vaccine)
- Need for Re-Vaccination & Interval: Protein-based RSV Vaccines Appear to Have Durable Efficacy for ~2 Seasons, Indicating Need for Re-vaccination Every ~2 Years
- Opportunity for New Players: GSK/Pfizer Re-vaccination Data has been Unsuccessful to-date, Potentially Due to T4-Foldon Tag Immune Interference; Large Opportunity for New Players if Re-vaccination Issue can be Overcome



- Maternal Immunization: Infant Market Expected to be Dominated by RSV mAbs
- High-Risk/Co-Morbidities (5-59 Years): Limited to People with High-Risk Conditions



✓ Validated Market: ~\$2.5Bn Sales in 1st Year of Launch; ex-U.S. Markets Still Untapped

- After existing older adult population (prevalence) is fully-penetrated, 'initial dose' market will mainly be for people newly-entering age cohort each year (incidence)
- Despite existing products in this indication, significant opportunity for differentiated products with best-in-class profile (improved safety/tolerability while maintaining durable efficacy); ability to re-vaccinate provides convenience advantage, avoiding need for brand switching after initial dose







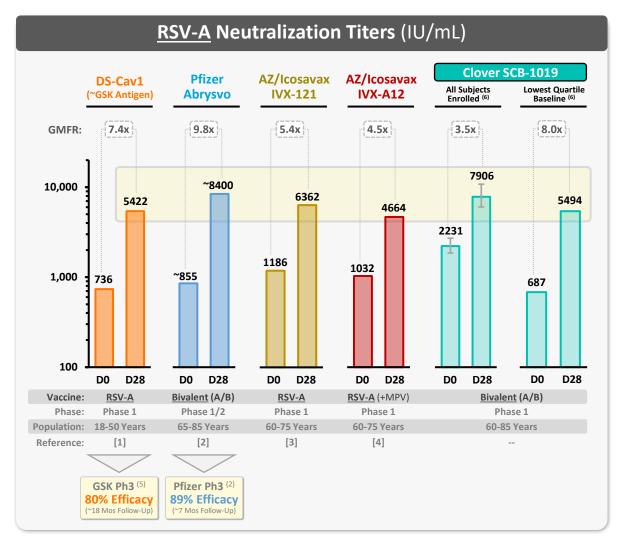
Respiratory Combination Vaccine Lifecycle Management (LCM) Opportunities

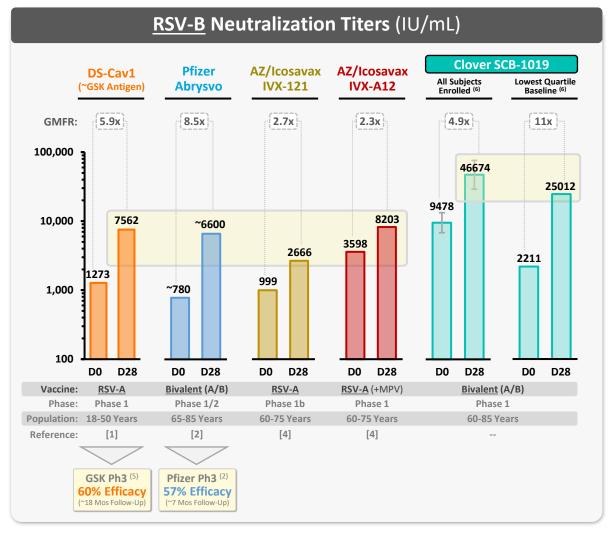
- Respiratory Combination Vaccines are Expected to Take Significant Future Market Share, Given Broader Coverage & Convenience if Successfully Developed
- Many LCM Precedents for Combination, Higher-Valency, or Improved Vaccines Taking Majority Market Share (>60%), Including Pediatric Combo vs DTaP, HPV9 vs HPV2/4, Seasonal Flu QIV vs TIV, RotaTeg 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)
- hMPV and/or PIV3: 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





SCB-1019 Phase 1 Results in Older Adults are In-Line or Potentially Favorable to Other RSV PreF Protein Vaccines





☑ SCB-1019 Potentially In-Line

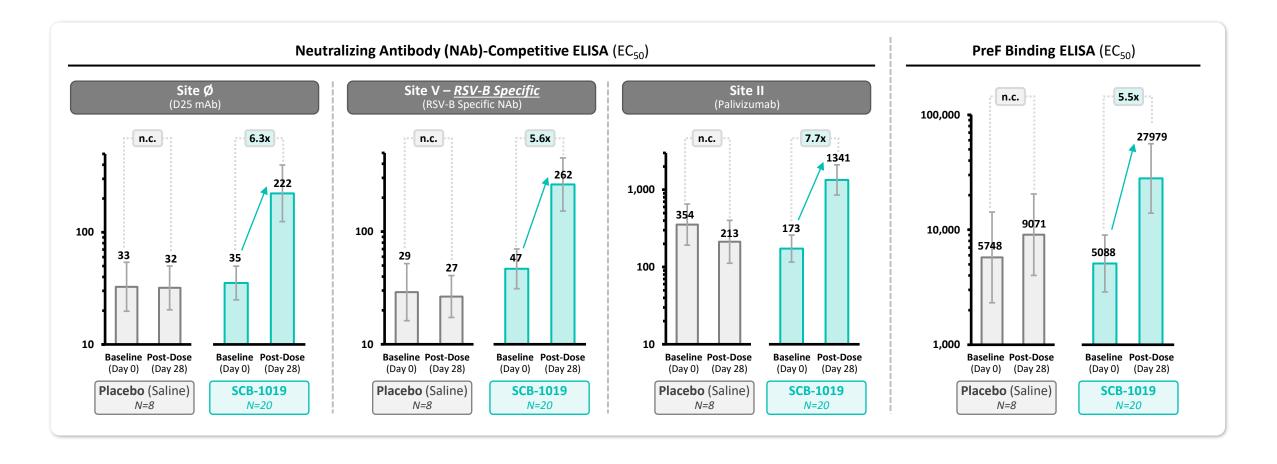
SCB-1019 In-Line or Potentially Favorable

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). Phase 1 data shown for SCB-1019 at the selected dose level. Bars represent GMTs (± 95% confidence intervals). Abbreviations: IU/mL (International Units Per Milliliter), GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise).
[1] DOI: 10.1016/S2213-2600(21)00098-9 (data for 150µg group shown), [2] Pfizer FDA VRBPAC Meeting Presentation FEB 28, 2023 (data for 120µg group shown), [3] Icosavax Company Presentation JUN-28-2022 (data for 75µg group shown), [4] Icosavax Company Presentation MAY 22, 2023 (data for 225µg group shown). [5] DOI: 10.1093/cid/ciae010. [6] 20 subjects were enrolled at selected SCB-1019 dose level. Stratified analysis for bottom quartile (n=5) based on baseline RSV neutralization titers are shown.



SCB-1019 Preliminary Phase 1 Results (Older Adult Cohort)

- Significant increase in Site Ø and Site V NAb-Competitive Titers further confirm SCB-1019 antigens being stabilized in prefusion form
- Exploratory ELISA assay results provide additional evidence of robust immune response induced by SCB-1019

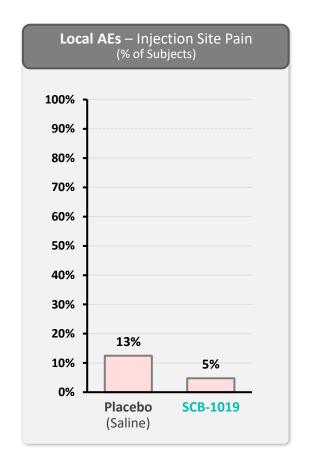


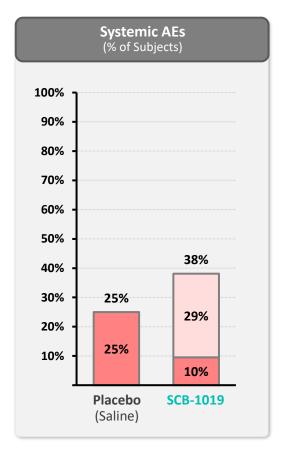


SCB-1019 Preliminary Phase 1 Results (Older Adult Cohort)

Safety & Reactogenicity Results

- ✓ <u>Favorable</u> Safety & Reactogenicity Observed for SCB-1019 Formulation and <u>Comparable</u> to <u>Placebo</u> (Saline)
- ✓ Local and Systemic Adverse Events (AEs) were Generally Mild & Transient (Most Common AEs were Injection Site Pain, Headache, Fatigue)
- ✓ No Serious Adverse Events (SAEs), AEs of Special Interest (AESIs), or AEs Leading to Discontinuation were Observed



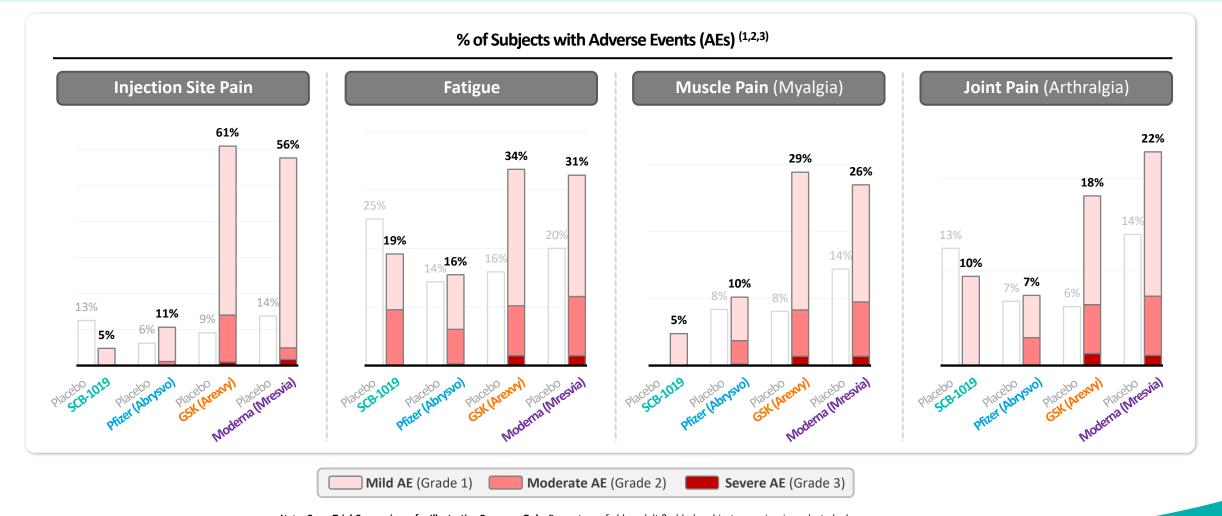






Potential Best-in-Field Tolerability Profile

- Potential Differentiated & Favorable Tolerability Profile for SCB-1019 Compared to Currently-Approved Oil-in-Water Adjuvanted (2) and mRNA (3) RSV Vaccines
- Important Consideration for Vaccine Uptake, Especially for Potential Targeted Populations (Children & Elderly)





Executive Summary

- **☑** Positive Preliminary Phase 1 Immunogenicity & Safety Results for Bivalent RSV Vaccine Candidate SCB-1019 in Older Adult Cohort
- ☑ 1st RSV PreF Vaccine Candidate Developed in China to Enter the Clinical Trial Stage and Generate Clinical Data
- ☑ Results in Older Adults & Elderly (60-85 Years) are Consistent with Earlier Results in Younger Adults (18-59 Years)
- Study Design: The Phase 1 Clinical Trial in Australia is a Randomized, Placebo-Controlled Study to Assess the Safety, Reactogenicity and Immunogenicity of SCB-1019
 - **48 Older Adult Subjects** were enrolled, and received SCB-1019 or saline placebo
- Positive Immunogenicity Results in Older Adults: Bivalent SCB-1019 Significantly Boosted RSV-A and RSV-B Neutralization Titers Up to 7,906 IU/mL and 46,674 IU/mL, Respectively
 - High baseline nAb titers at Day 0, especially to RSV-B, were observed, potentially reflecting recent outbreaks near the clinical trial sites
 - Up to <u>8-fold (RSV-A nAb)</u> and <u>11-fold (RSV-B nAb)</u> Geometric Mean Fold Rises (GMFRs) were observed for sub-analyses in subjects with the lowest quartile baseline nAb titers
 - Clover's preliminary immunogenicity data across both RSV-A and RSV-B neutralization appear to be in-line or potentially favorable compared to other top-tier protein subunit RSV PreF vaccines
- Safety & Reactogenicity: SCB-1019 Demonstrated a Favorable Safety & Reactogenicity Profile Comparable to Saline Placebo
 - No serious adverse events (SAEs), adverse events of special interest (AESIs), or AEs leading to discontinuation were observed
- Full Phase 1 Data Readout is Expected by the End of 2024



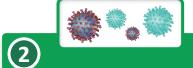
SCB-1019 is a Potential Best-in-Field & Differentiated RSV Vaccine Globally

- Clover Poised to be a Leader in RSV Vaccine Market in China, with Global Competitive Edge Potential
- Clover is addressing the high technical hurdles for RSV vaccine development, utilizing our unique in-house technology platform, for potential long-term differentiation



Differentiated Stabilized PreF-Trimer

- ✓ Stabilization of Prefusion F (PreF)
 Trimer Critical for RSV Vaccines (1)
- ✓ SCB-1019 is utilizing proprietary stabilizing Mutations & Trimer-Tag platform technology; confirmed as stable PreF-Trimer
- ✓ Preclinical studies indicate SCB-1019 PreF stabilization is competitive to DS-Cav1 (PreF antigen utilized in GSK and Icosavax RSV vaccines)
- ✓ Preclinical and Phase 1 clinical studies confirm SCB-1019 has stable PreF conformation inducing significant RSV neutralizing antibody responses



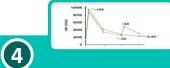
Immunological Breadth (RSV-A + RSV-B)

- ✓ Immunological Breadth is Needed Against Both RSV-A & RSV-B (2 groups co-circulate & alternate in prevalence across seasons)
- Monovalent RSV-A vaccines (GSK & Icosavax) observed suboptimal breadth & durability trends against RSV-B in clinical trials (2)
- ✓ SCB-1019 bivalent RSV-A/B approach is designed to induce broad neutralization against both RSV-A & RSV-B, demonstrated in Phase 1 & preclinical studies



Potential Best-in-Field Safety & Tolerability

- Safety & tolerability important to maximizing vaccine uptake, especially for target populations for RSV (young children & elderly)
- ✓ Oil-in-water emulsion adjuvanted protein-based vaccines & mRNA vaccines have observed higher rates of adverse events, which may limit development scope and market uptake in young children
- ✓ Potential for SCB-1019 to show best-in-field safety & tolerability profile (oil-in-water emulsion adjuvant not utilized in SCB-1019)



Re-Vaccination Ability (No Immune Interference)

- ✓ Potential to satisfy need for repeated annual seasonal boosting; humanderived Trimer-Tag technology has demonstrated boosting & has not observed immune interference previously
- GSK observed lack of efficacy after second dose in Year 2 in Phase III study (with suboptimal increase in RSV neutralizing antibody levels)
- Potentially associated with GSK & Pfizer trimerization technology: non human-derived T4 Foldon may induce ADA against T4 Foldon interfering with PreF immune responses



Potential LCM to Develop Respiratory Combo Vaccine

- ✓ Potential to develop 'Respiratory
 Combination Vaccines' across
 Mononegavirales order of viruses
 (RSV / hMPV / PIV3), utilizing RSV as
 the 'anchor'
- ✓ Trimer-Tag protein subunit has platform advantages for combo approach versus mRNA (combo dose is limited by safety) and VLP (complicated CMC)
- ✓ Can Leverage Clover's PreF stabilization & production experience
- ✓ Lifecycle management (LCM) opportunity for blockbuster RSV

✓ Differentiation for Potential Best-in-Class Efficacy & Safety Profile ☑ Potential Continued Differentiation& Lifecycle Management (LCM) Opportunities

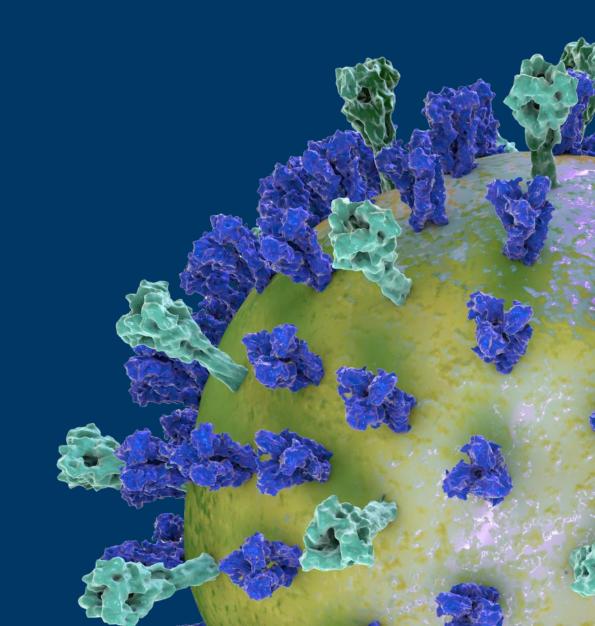
Note:

- (1) Taleb et al., Eur J Clin Microbiol Infect Dis., 2018 (<u>DOI</u>: 10.1007/s10096-018-3289-4). Besteman & Bont, Am J Respir Crit Care Me, 2019 (<u>DOI</u>: 10.1164/rccm.201901-0233ED).
- 2) GSK June 2023 ACIP presentation, NCT04732871. Icosavax Investor Update Presentation (08-AUG-2023)



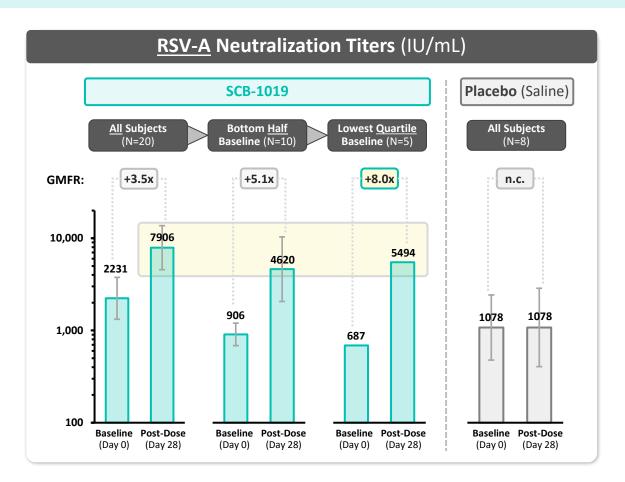


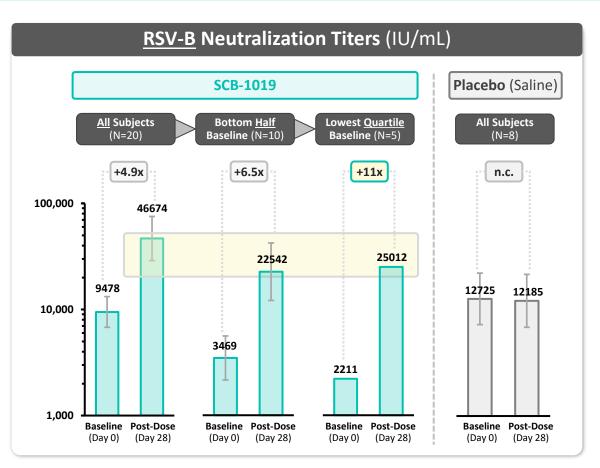
Appendix



SCB-1019 Preliminary Phase 1 Results (Older Adult Cohort)

- SCB-1019 Induced <u>Significant Increases</u> in RSV-A and RSV-B Neutralization Titers (at Day 28), <u>Despite High Titers at Baseline</u> (at Day 0)
 - High Baseline RSV Nab Titers, Especially to RSV-B, Potentially Reflecting Recent Outbreaks Near the Clinical Trial Sites
- GMFRs up to 8-fold (RSV-A) and 11-fold (RSV-B) for Sub-analysis in Subjects with the Lowest Quartile Baseline nAb Titers





Abbreviations: IU/mL (International Units Per Milliliter), GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise).

Note: Bars represent GMTs (± 95% confidence intervals). Data shown for SCB-1019 subjects enrolled at the selected dose level.

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.



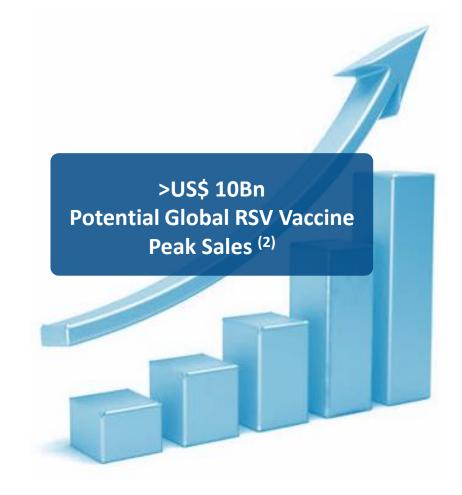
☑ Global Commercial Opportunity of RSV Vaccine has been Validated: *Product Sales in First Season of Launch (H2-2023) Beats Expectations*

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

Global RSV vaccine sales reached ~US\$ 2.5Bn in the first season of commercial launch in H2-2023

(<u>H2 2023</u>: ~US\$ 1.5 billion for GSK Arexvy and ~US\$ 890 million for Pfizer Abrysvo ⁽¹⁾)

- ~40-50% of people who received RSV vaccine were coadministered with Flu±COVID vaccines, demonstrating the commercial synergies of respiratory vaccines
- **Premium Pricing Achieved: ~US\$ 300/dose**



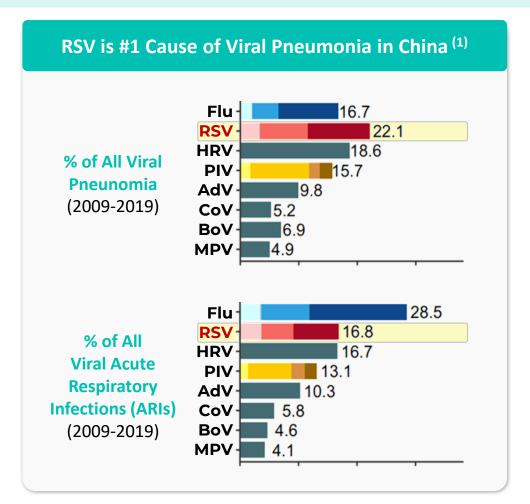


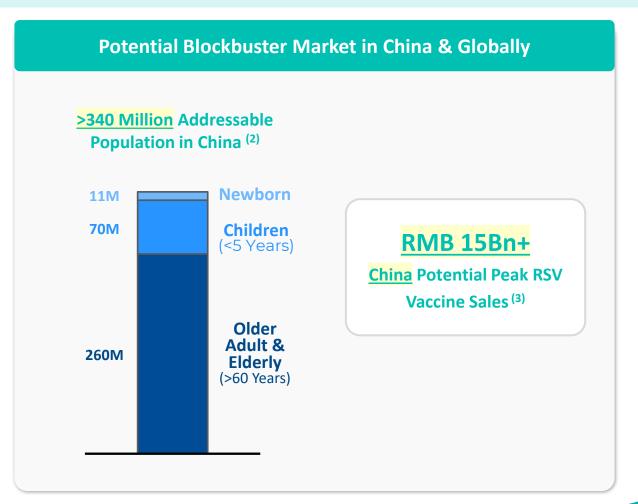
⁽¹⁾ GSK and Pfizer Q3 2023 and FY 2023 results announcements

⁽²⁾ Wall Street Investment Bank Research has released forecasts for the global RSV vaccine market for the elderly, among them Cowen Research – US\$13Bn (Feb 2023), Jefferies – US\$15Bn (Jul 2023).

Potential Blockbuster RSV Vaccine Market in China & Globally

- RSV is the leading cause of viral pneumonia in China, with an addressable population of >340 million
- Blockbuster China Opportunity Wide Open: Clover has the first RSV PreF vaccine developed in China to enter clinic stage and the first to generate clinical data





Abbreviations: Flu (influenza virus), HRV (human rhinovirus), PIV (human parainfluenza virus), AdV (human adenovirus), CoV (human betacoronavirus), BoV (human bocavirus), MPV (human metaneumovirus).

(1) Li et al., Nat. Commun., 2021 (DOI: 10.1038/s41467-021-25120-6).

(2) China demographics in 2021.

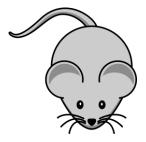
(3) Illustrative projection assuming RSV vaccine market of ~50 million doses annually at peak (approximately half of flu vaccine market) and average blended pricing in China of RMB 350 per dose (pricing in between flu vaccine [~RMB 120-200/dose] and pneumococcal conjugate vaccines [~RMB 550-700/dose]).

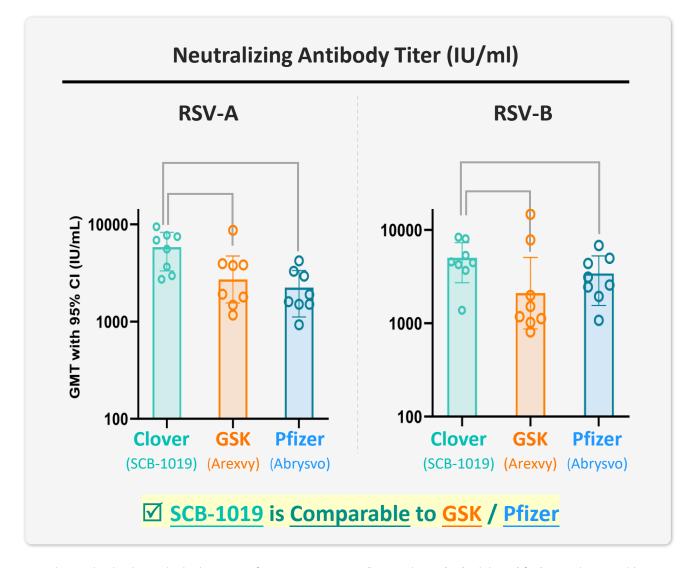
(4) Wall Street research estimates for global older adult RSV vaccine market, including Cowen Research – US\$13Bn (Feb 2023), Jefferies – US\$15Bn (Jul 2023).





Clover (SCB-1019) vs. GSK (Arexvy) vs. Pfizer (Abrysvo)



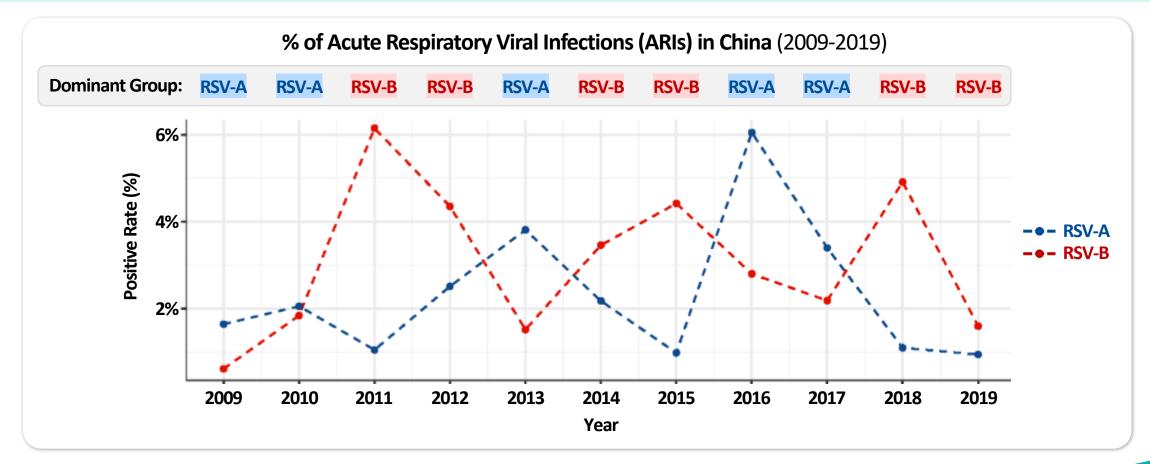


Note: Clover preclinical studies. Head-to-head comparison of SCB-1019 versus commercially-procured Arexvy (GSK) and Abrysvo (Pfizer) in primed mouse model. Mice were primed with live RSV-A virus, and after approximately 3 months, mice were given a single dose of vaccine (Day 0). Sera were collected on 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.



2 Broad Protection: RSV-A & RSV-B

- 2 main RSV groups (RSV A and RSV B) typically co-circulate and alternate in prevalence across seasons
- > Thus, it is important for RSV vaccines to induce broad & durable protection against both groups
- > Amino acid sequence differences on F antigen may result in different neutralizing antibody binding epitopes, indicating antibody epitopes form strain-specific sequence and configuration under the pressure of immune selection



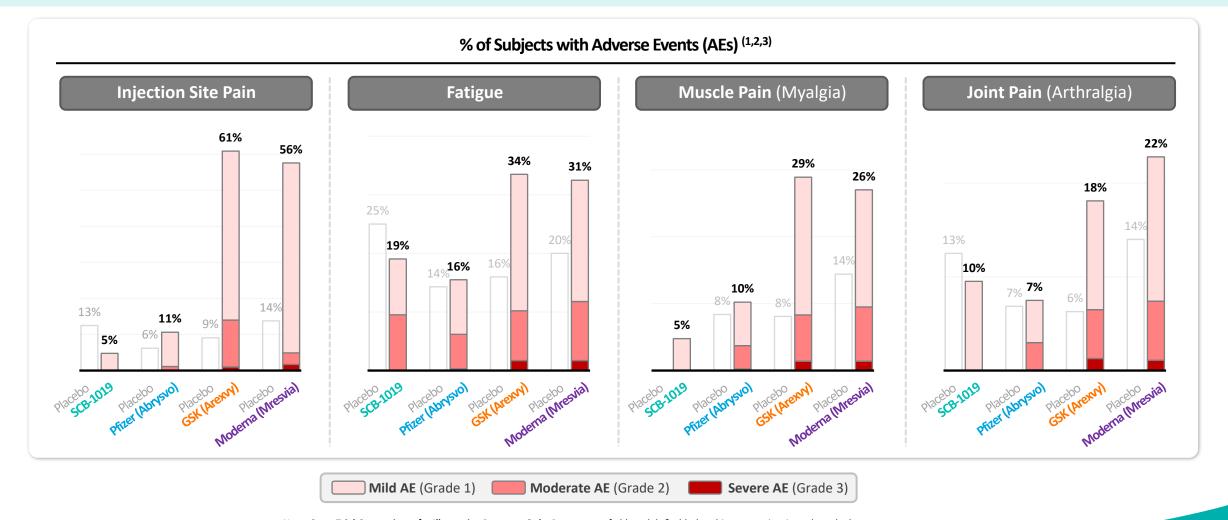
Note: Viral composition tested in 110,058 patients with ARIs in the mainland of China from 2009–2019. Source: Li et al., Nature Communications, 2021 (DOI: 10.1038/s41467-021-25120-6).





Differentiation in Safety & Tolerability

- Potential Differentiated & Favorable Tolerability Profile for SCB-1019 Compared to Currently-Approved Oil-in-Water Adjuvanted (2) and mRNA (3) RSV Vaccines
- Important Consideration for Vaccine Uptake, Especially for Potential Targeted Populations (Children & Elderly)

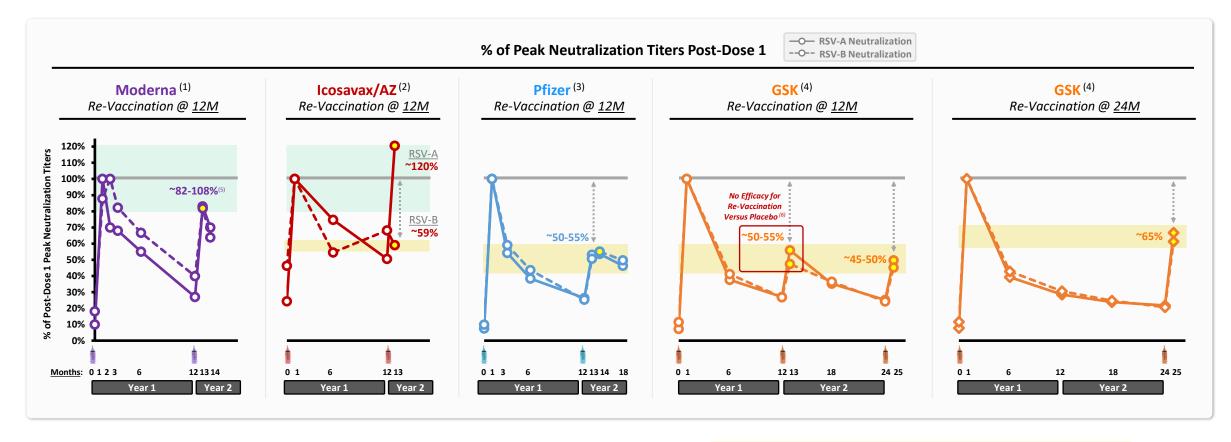






Re-Vaccination Issue for Vaccines Using T4-Foldon Tag (GSK/Pfizer)

- GSK/Pfizer: Neutralization Titers Only Reach 45-65% of Peak Levels 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 4-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</p>



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

[&]amp; CLOVER

⁽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).



Potential for Respiratory Combo Vaccine (RSV + PIV + MPV) LCM Opportunity

- Total Disease Burden of Combo (RSV+PIV+MPV) is similar or greater than Flu Globally and in China; combination vaccine is a compelling opportunity & unmet need
- Potential to directly leverage Clover's RSV experience to develop 'Respiratory Combo Vaccines' across mononegavirales order of viruses (RSV + PIV + MPV)
- <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)







Virus Order/ Disease

☑ All 3 are Part of Mononegavirales Order

✓ All 3 Cause **Symptomatic Respiratory Disease**

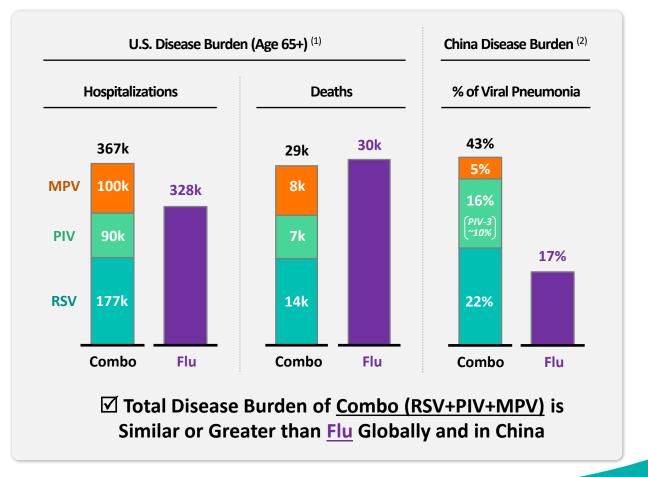
Antigen

✓ All 3 have Similar <u>Trimeric Fusion (F)</u> Antigen, Requiring Stabilization in Prefusion form (<u>PreF</u>)

Seasonality

✓ All 3 Observe Peak Outbreaks in Winter

At-Risk Populations



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.



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

Elderly RSV Vaccine Phase 3 Efficacy Durability: Summary Reference Data

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

	RSV			i zer (ABRYS\ I ≥3 Sympto			Moderna (MRESVIA) RSV-LRTD ≥3 Symptoms									
Phase 3 Median Follow-Up Time:	6.7 Months	12.0 Months	14.0 Months	17.8 Months	23.3 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)	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.)	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.)	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)	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							z er (ABRYS\ ≥2 Sympto			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	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)	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.)	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.)	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)	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).



⁽¹⁾ Severe RSV Endpoints: 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).

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</u> structure

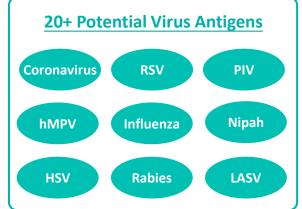




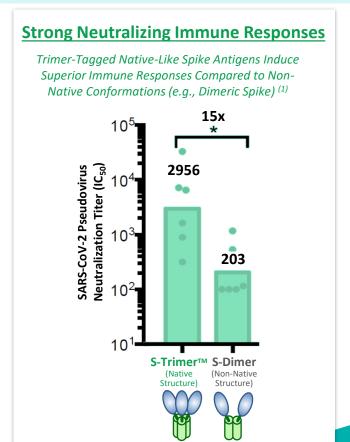
Trimer-Tag Technology Platform for Vaccine Development

- Platform for development of protein-based vaccines based on naturally-trimeric virus spike antigens
- 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 & precise neutralizing 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

Trimer-Tag Technology Platform Naturally Trimeric Virus Antigen Variable **Domain** Constant **Domain Trimer Tag**



- √ 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



1) SARS-COV-2 pseudovirus neutralizing antibody responses in mice vaccinated with two doses of 5-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

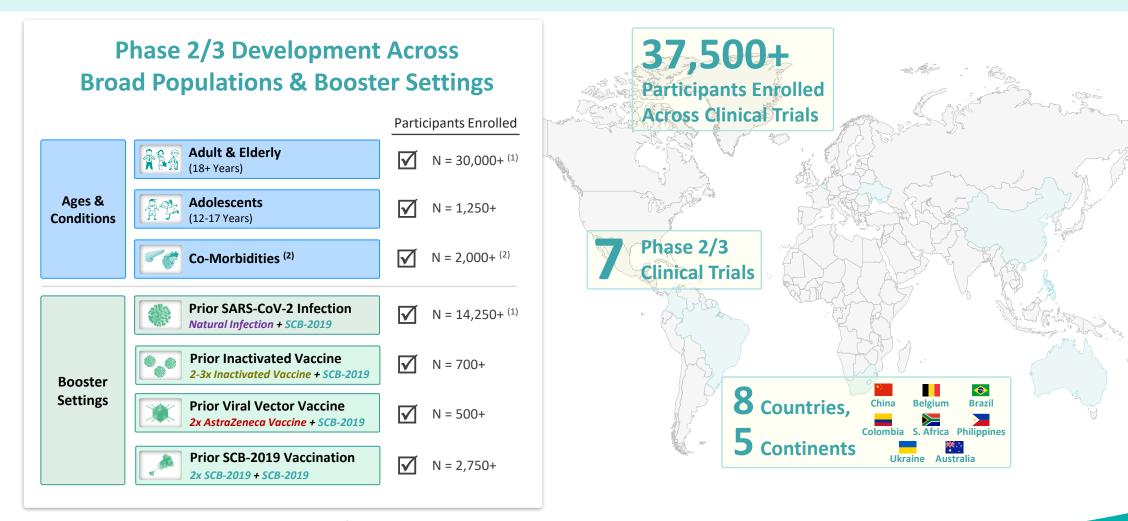


lote: Representative list of viruses with naturally trimeric spike antigens is illustrative and not exhaustive. Abbreviation: ADA (Anti-Drug Antibodies).

^{*} A "timer" refers to a molecule or an anion formed by combination or association of three molecules or income the same substance. Trimerization is a chemical reaction that uses three identical molecules to proacte 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 imple parts are referred to as "timerired to as timerired to as "timerired to as "timerired to as "timerired to as timerired to as "timerired to as timerired to as "timerired to as timerired to as "timerired to as timerired t

Trimer-Tag: Extensive Experience from Clinical Studies Globally

- **✓** Vaccination experience in broad population groups (elderly, adult, adolescent and people with co-morbidities)
- Only Chinese vaccine company ever granted clinical trial approval in Europe



^{30,128} total adult & elderly participants enrolled in Phase 2/3 SPECTRA trial, including 14,622 participants with evidence prior of SARS-CoV-2 infection.

⁽²⁾ Enrolled in Phase 2/3 SPECTRA trial; 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.



Recognized & Endorsed by Leading Scientific Institutions Globally









Trimer-Tag
technology has been
published multiple
times in the most
renowned scientific
journals globally
(Including Lancet)

















Received US\$ 397million funding from CEPI to support Clover establishing its vaccine platform (Trimer-Tag Platform + Vaccine Manufacturing Capabilities)





Thank You!