



**SCB-1019 (Bivalent RSV PreF-Trimer):**  
*Phase 1 Older Adult & Elderly Cohort Data*

**June 18<sup>th</sup>, 2024**

# Executive Summary

- ✓ **Positive Preliminary Phase 1 Immunogenicity & Safety Results for Bivalent RSV Vaccine Candidate SCB-1019 in Older Adult Cohort**
- ✓ **1<sup>st</sup> 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 **8-fold (RSV-A nAb)** and **11-fold (RSV-B nAb)** 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

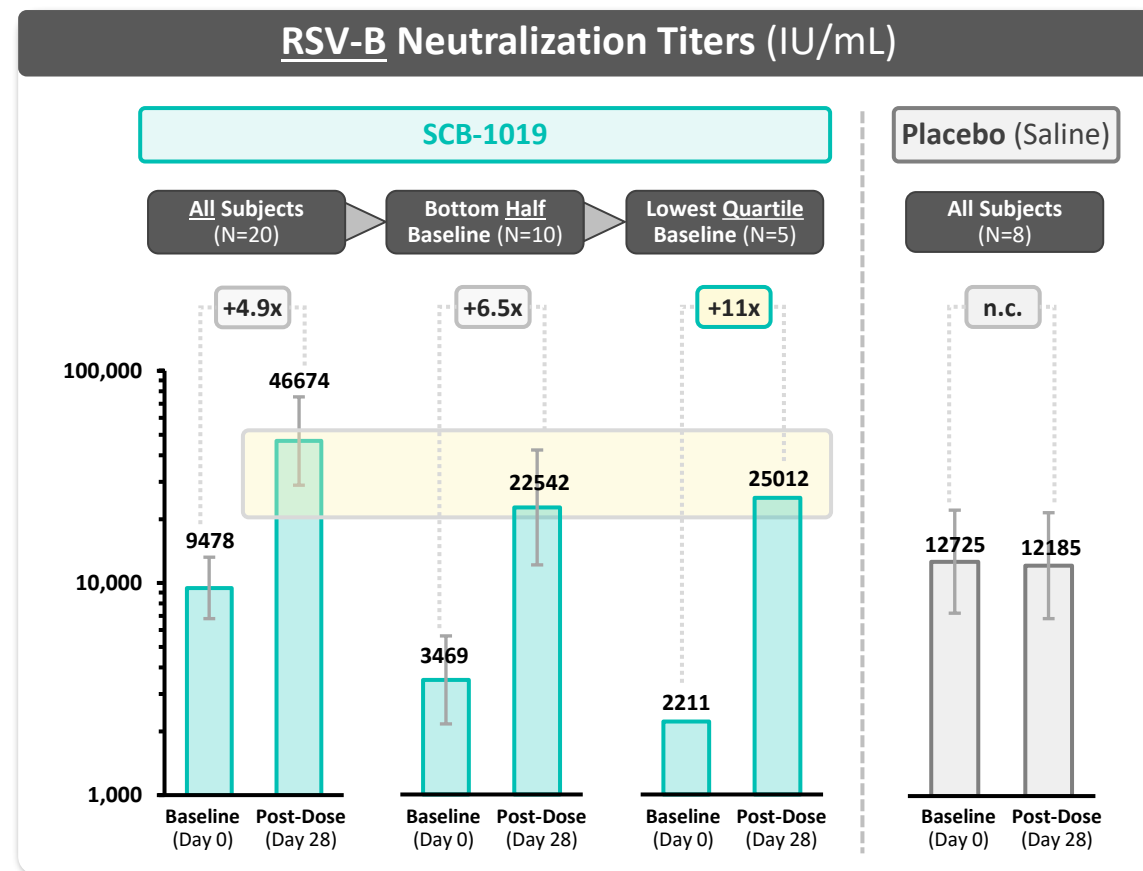
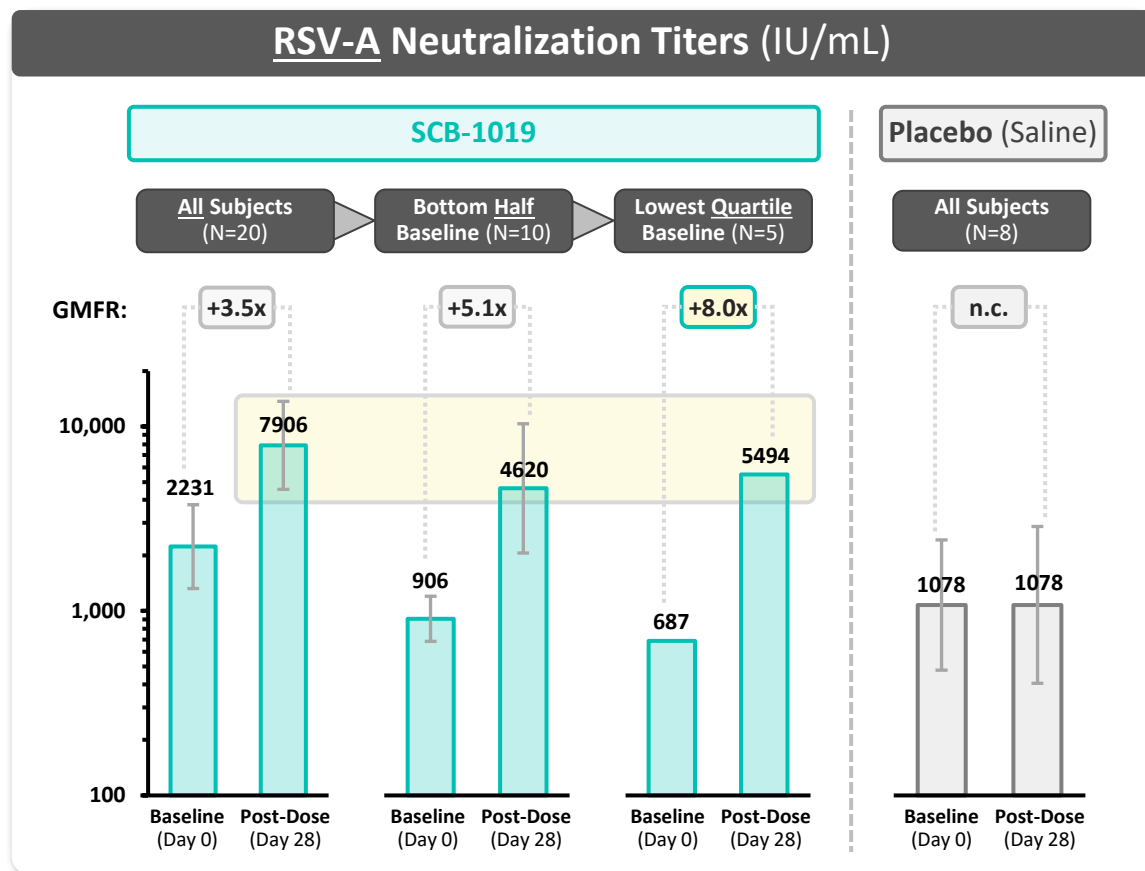
- **Safety & Reactogenicity: SCB-1019 Demonstrated a Favorable Safety & Reactogenicity Profile Comparable to Saline Placebo**

- 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 Preliminary Phase 1 Results (Older Adult Cohort)

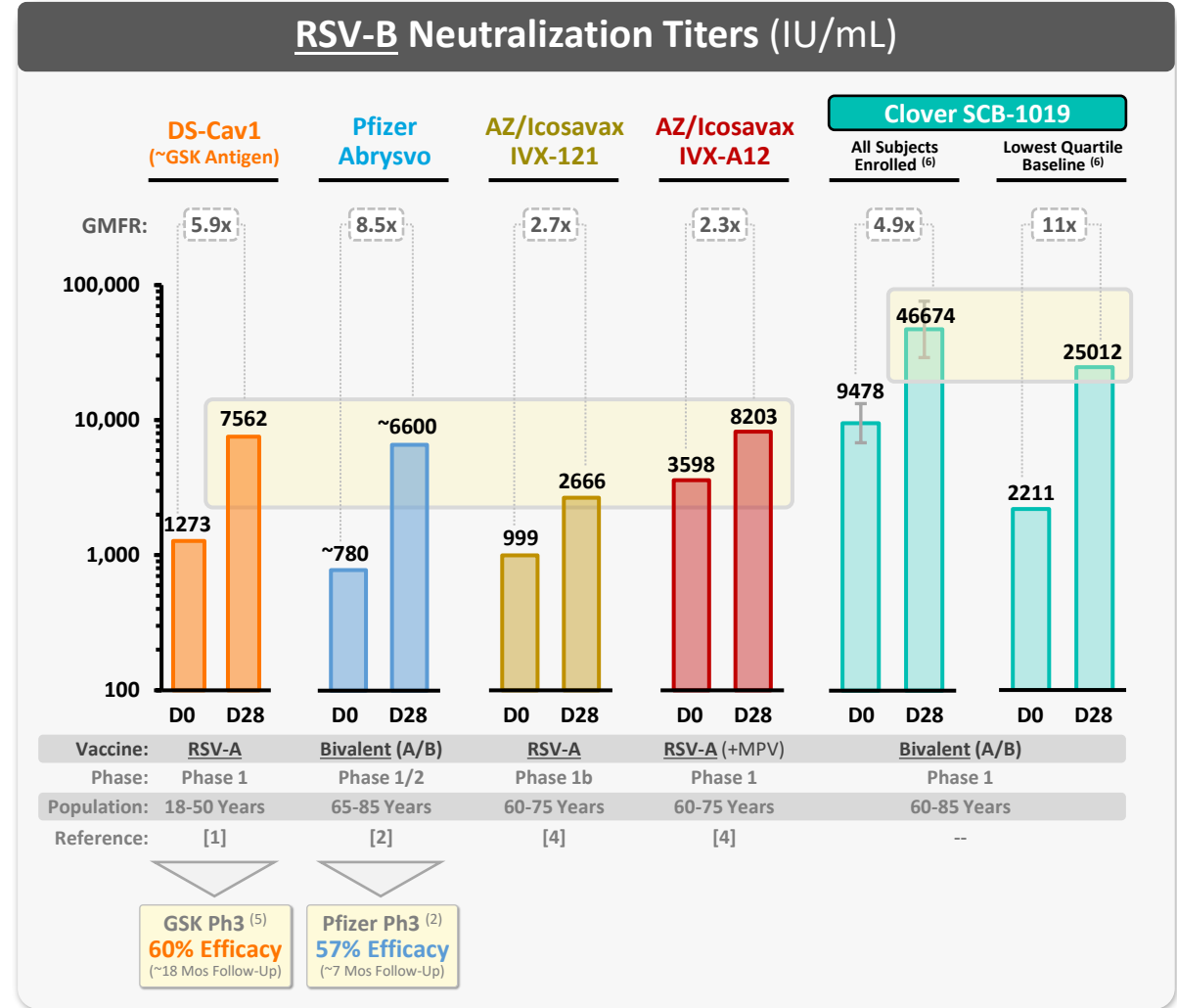
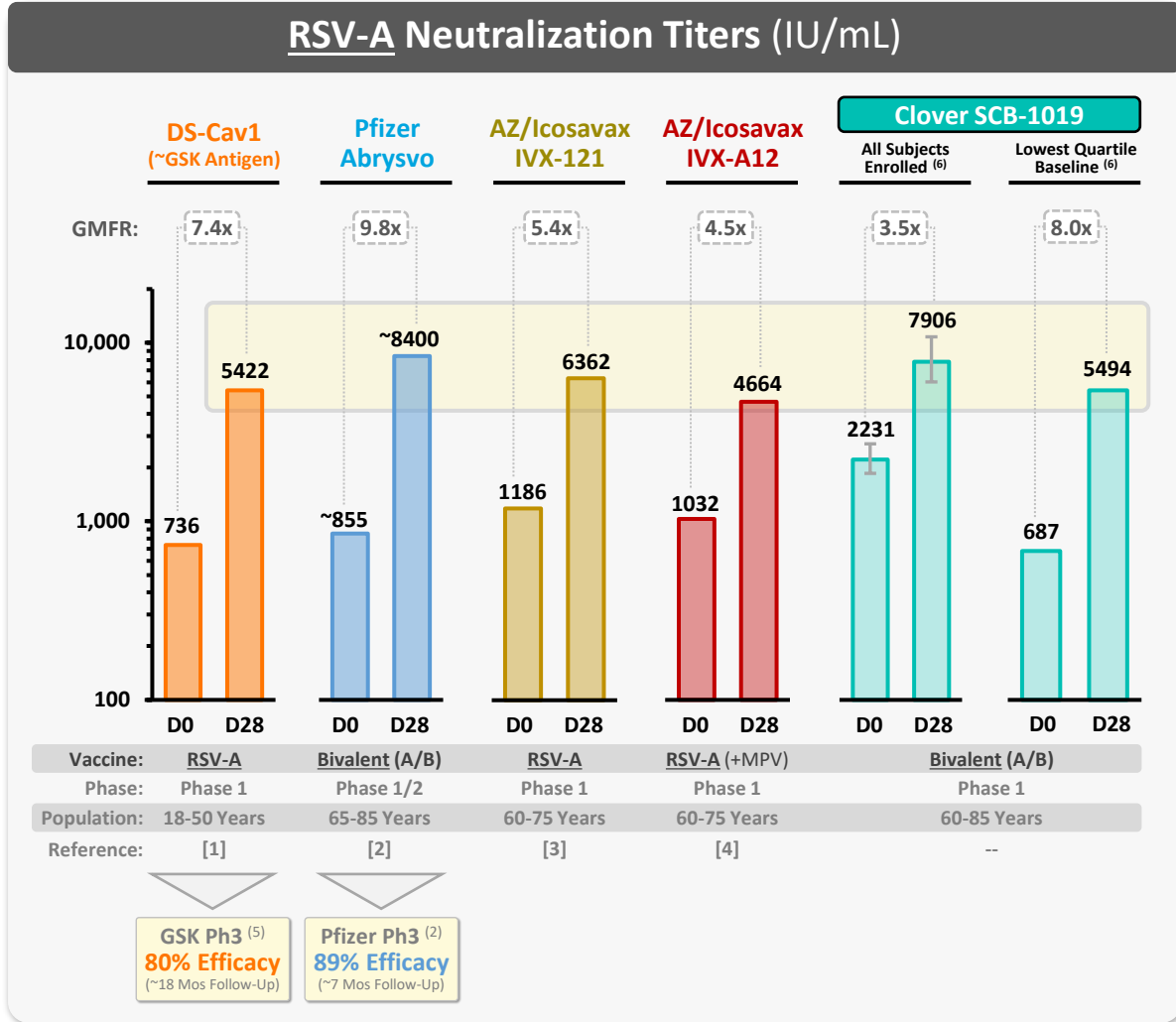
- SCB-1019 Induced Significant Increases in RSV-A and RSV-B Neutralization Titers (at Day 28), Despite High Titers at Baseline (at Day 0)
  - High Baseline RSV Nab Titers, Especially to RSV-B, Potentially Reflecting Recent Outbreaks Near the Clinical Trial Sites
- GMFRs up to 8-fold (RSV-A) and 11-fold (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 ( $\pm$  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.

# 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**

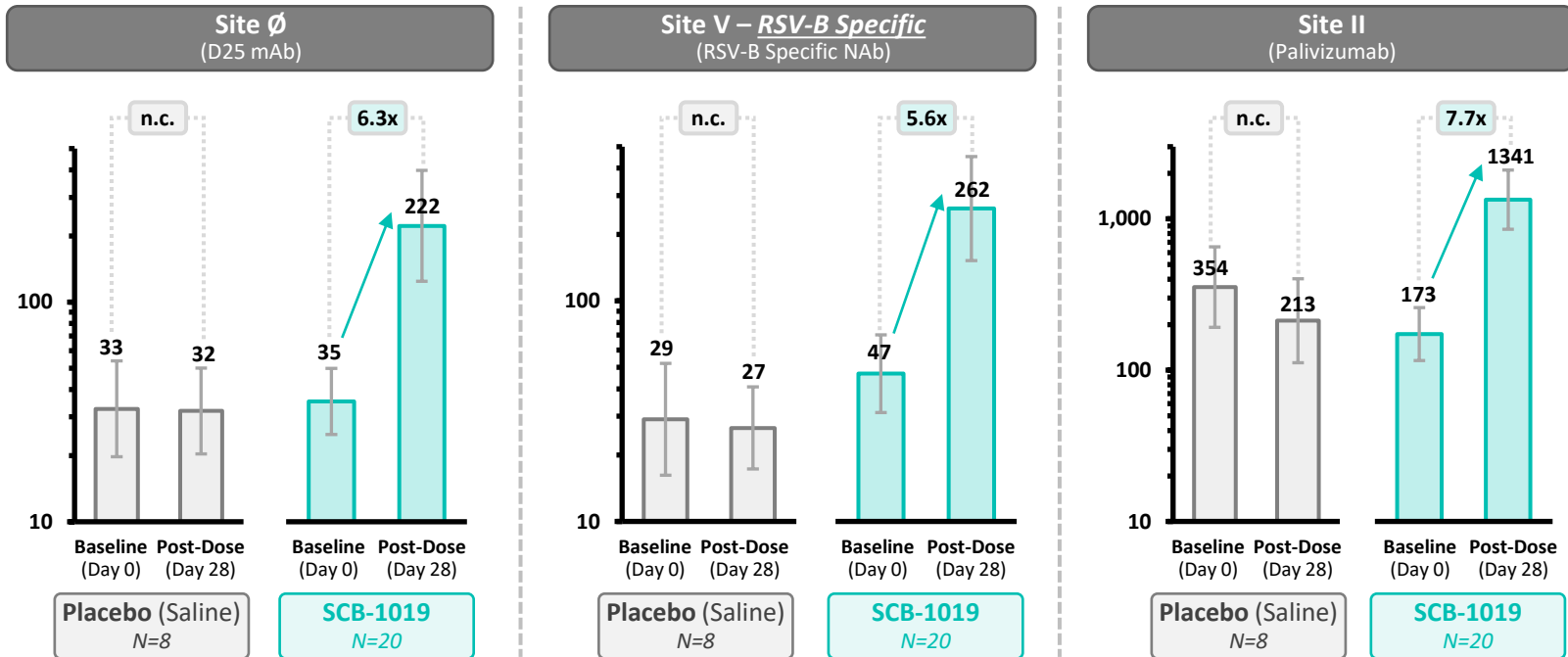
✓ **SCB-1019 In-Line or Potentially Favorable**

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.

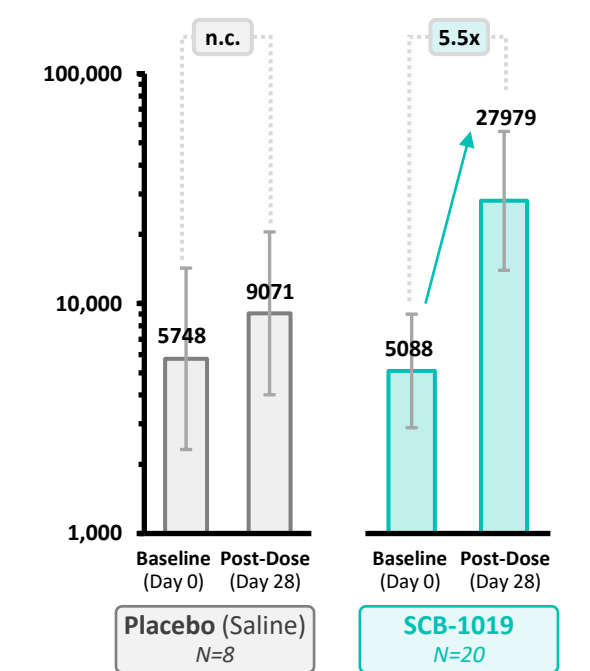
# SCB-1019 Preliminary Phase 1 Results (Older Adult Cohort)

- 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

## Neutralizing Antibody (NAb)-Competitive ELISA (EC<sub>50</sub>)



## PreF Binding ELISA (EC<sub>50</sub>)

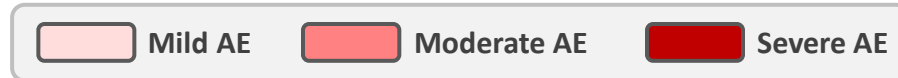
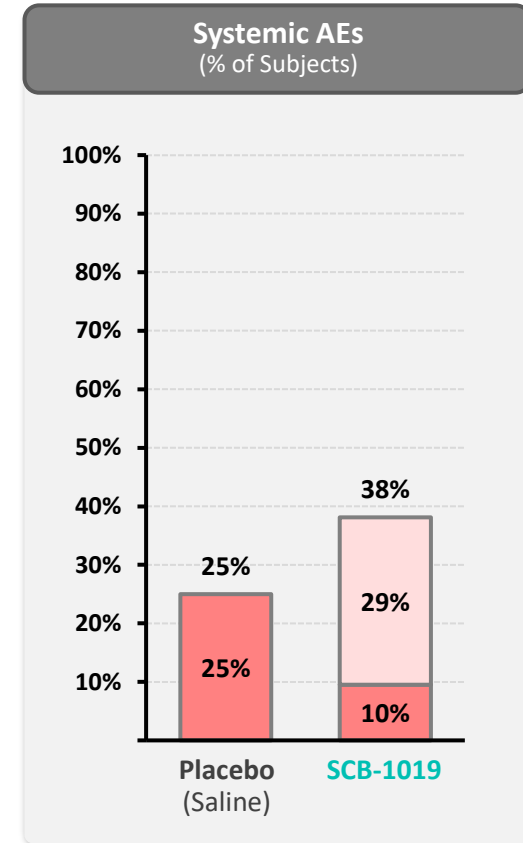
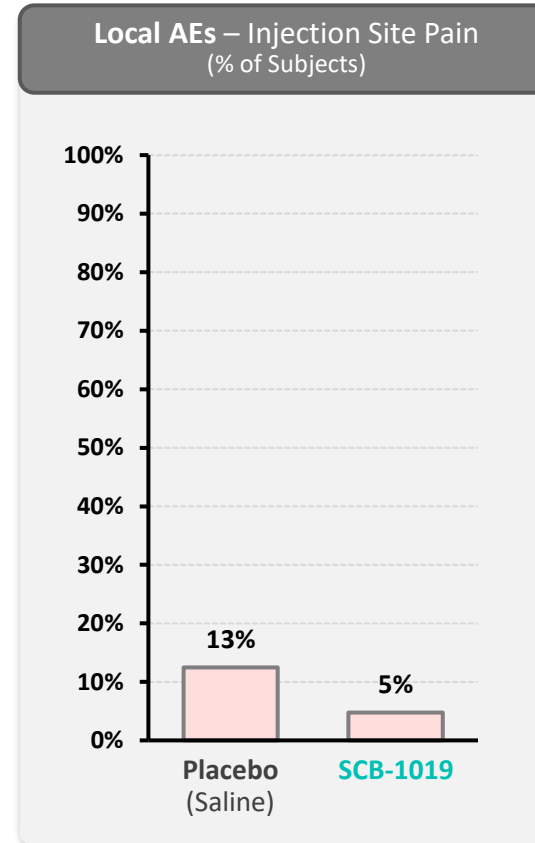


Note: Bars represent GMTs (± 95% confidence intervals). Results shown for exploratory ELISA assays. Phase 1 data shown for SCB-1019 subjects enrolled at the selected dose level. Abbreviations: GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise).

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

## Safety & Reactogenicity Results

- ✓ **Favorable Safety & Reactogenicity Observed for SCB-1019 Formulation and Comparable to Placebo (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**

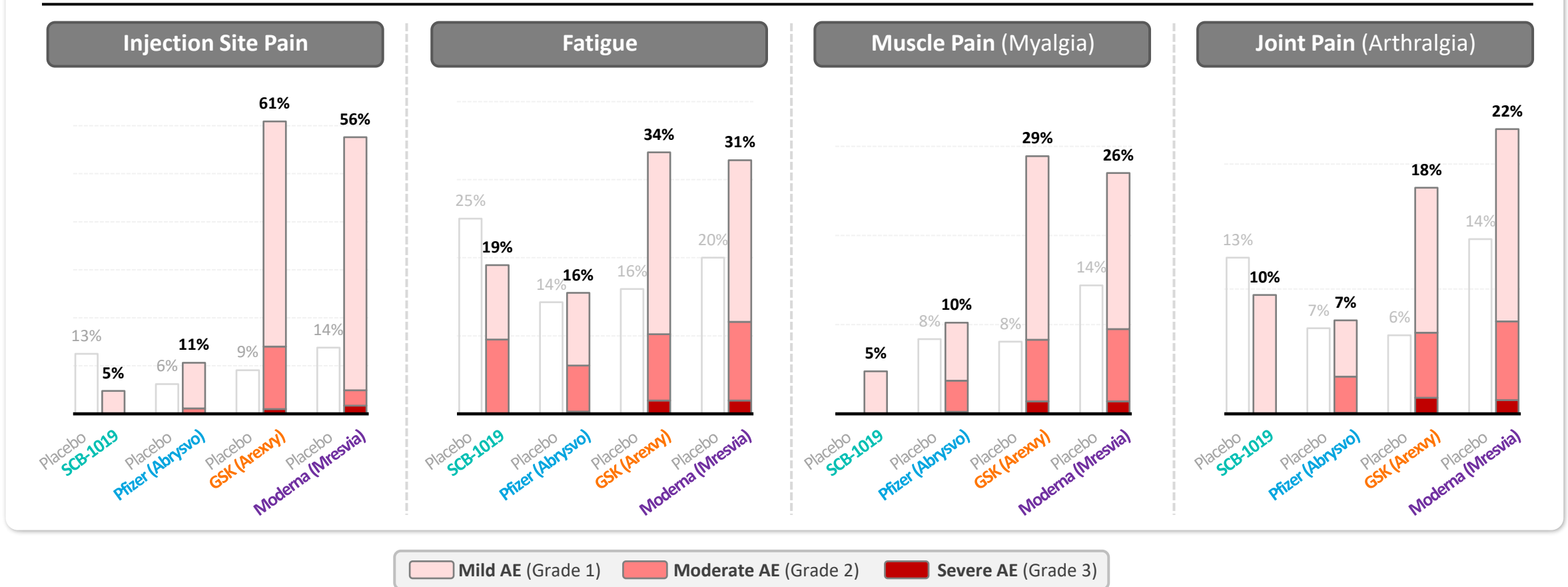


Note: **Cross Trial Comparisons for Illustrative Purposes Only.** Percentage of older adult & elderly subjects experiencing selected adverse events (AEs) following vaccination with RSV vaccine or placebo in clinical trials. Phase 1 data shown for SCB-1019.  
Sources: (1) 2023 Pfizer VRBPAC Meeting – FDA Briefing Document. (2) 2023 GSK VRBPAC Meeting – Sponsor Briefing Document. (3) Moderna February 2024 ACIP presentation (April 11, 2023).

# Potential Best-in-Field Tolerability Profile

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

% of Subjects with Adverse Events (AEs)<sup>(1,2,3)</sup>

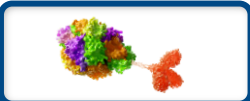


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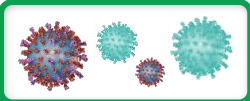
# SCB-1019 is a Potential Best-in-Field & Differentiated RSV Vaccine Globally

- ✓ 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




**1**  
**Differentiated Stabilized PreF-Trimer**

- ✓ **Stabilization of Prefusion F (PreF) Trimer Critical for RSV Vaccines** <sup>(1)</sup>
- ✓ 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**



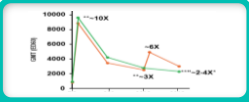
**2**  
**Immunological Breadth (RSV-A + RSV-B)**

- ✓ **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 <sup>(2)</sup>
- ✓ **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**




**3**  
**Potential Best-in-Field Safety & Tolerability**

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



**4**  
**Repeated Dosing Ability (No Immune Interference)**

- ✓ **Potential to satisfy need for repeated annual seasonal boosting**; human-derived **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**



**5**  
**Potential LCM to Develop Respiratory Combo Vaccine**

- ✓ Potential to develop '**Respiratory Combination Vaccines**' across Mononegavirales order of viruses (**RSV + PIV3 + MPV**), 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** experience for PIV3/MPV
- ✓ Lifecycle management (LCM) opportunity for blockbuster RSV

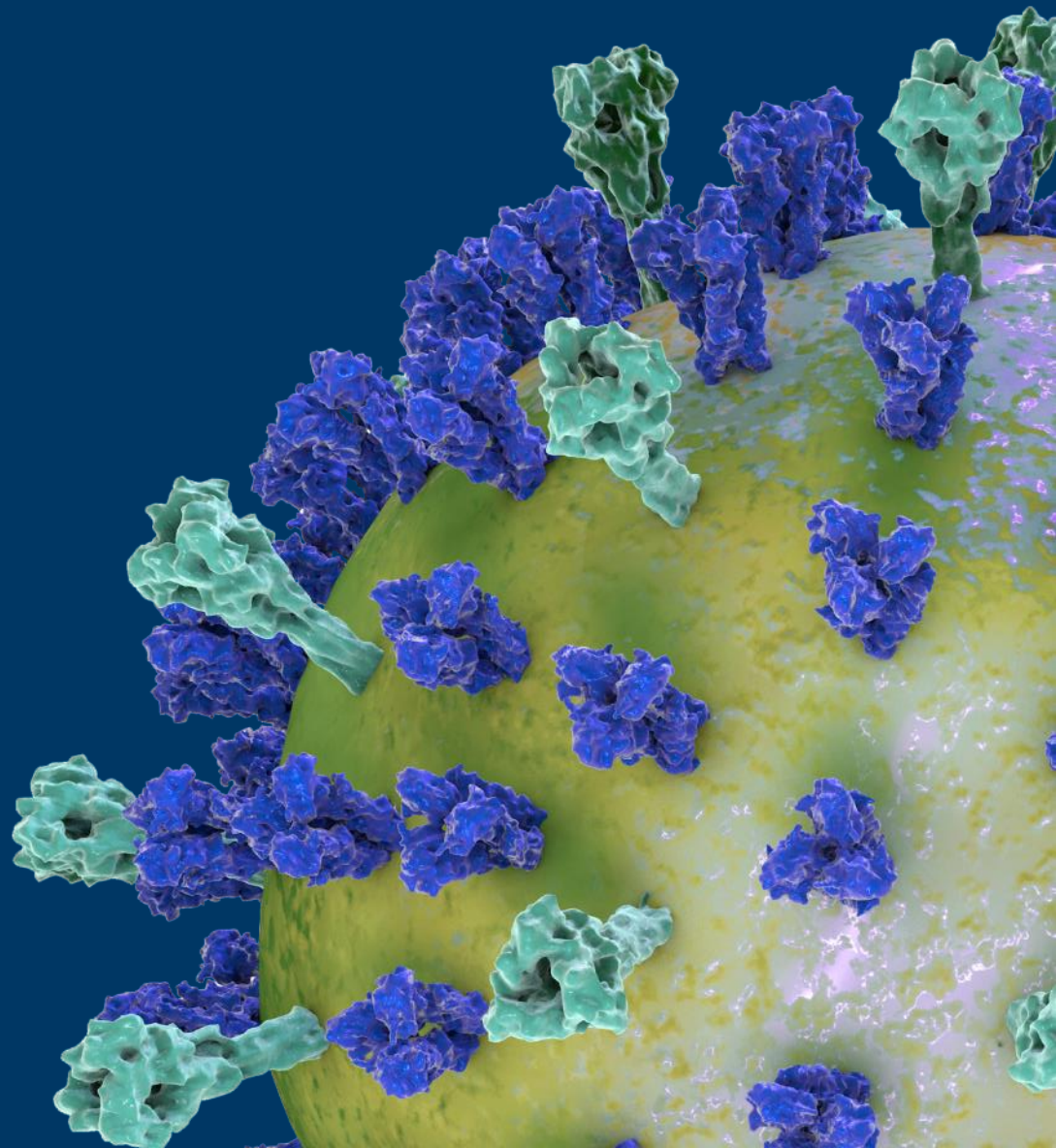
✓ **Differentiation for Potential Best-in-Class Efficacy & Safety Profile**

✓ **Potential Continued Differentiation & Lifecycle Management (LCM) Opportunities**

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



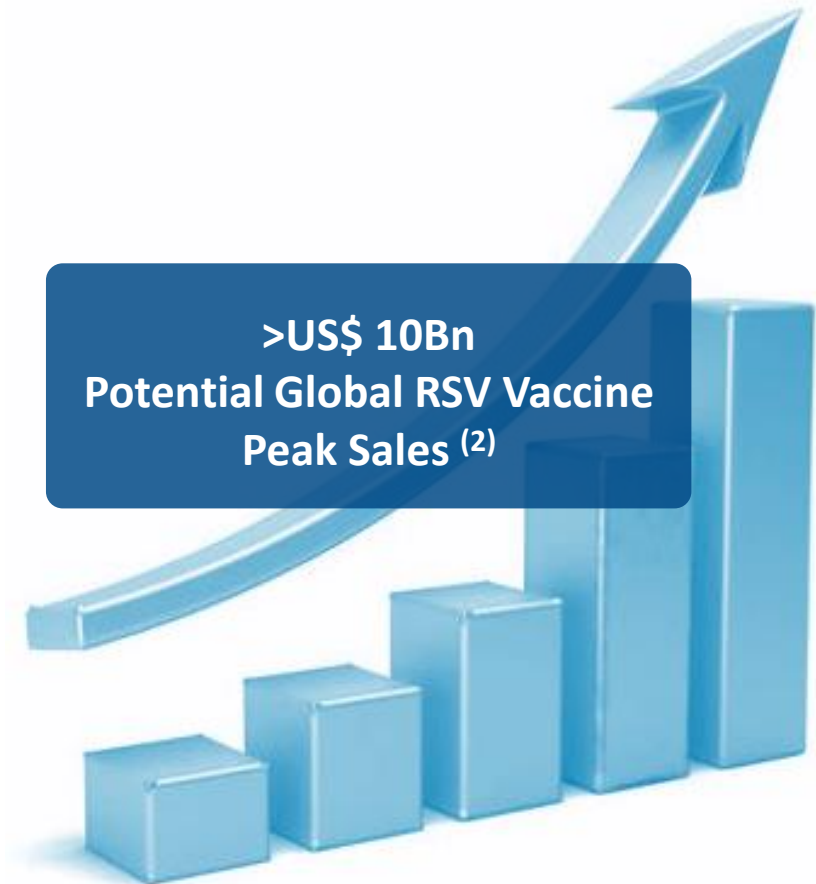
# Appendix



# ✓ 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**  
(H2 2023: ~US\$ 1.5 billion for GSK Arexvy and ~US\$ 890 million for Pfizer Abrysvo <sup>(1)</sup>)
- ✓ **~40-50% of people who received RSV vaccine were co-administered with Flu ± COVID vaccines, demonstrating the commercial synergies of respiratory vaccines**
- ✓ **Premium Pricing Achieved: ~US\$ 300/dose**



(1) GSK and Pfizer Q3 2023 results announcements

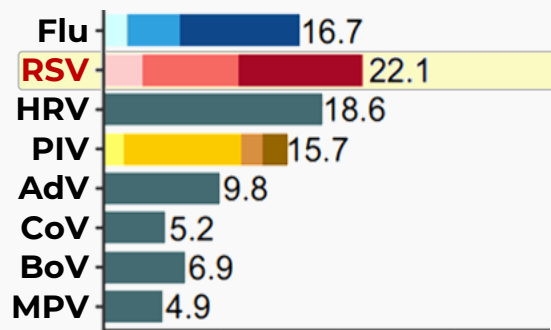
(2) Wall Street Investment Bank Research has released forecasts for the global RSV vaccine market for the elderly , among them Cowen Research – US\$13Bn (Feb 2023), Jefferies – US\$15Bn (Jul 2023).

# Potential Blockbuster RSV Vaccine Market in China & Globally

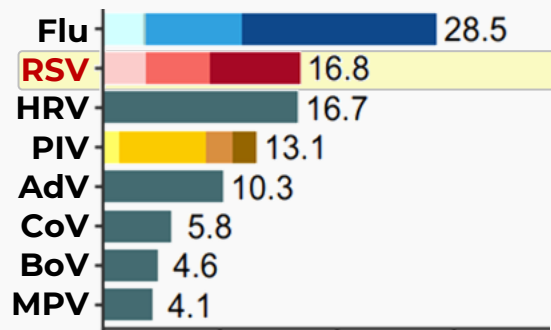
- ✓ RSV is the leading cause of viral pneumonia in China, with an addressable population of >340 million
- ✓ Blockbuster China Opportunity Wide Open: Clover has the first RSV PreF vaccine developed in China to enter clinic stage and the first to generate clinical data

## RSV is #1 Cause of Viral Pneumonia in China <sup>(1)</sup>

% of All Viral Pneumonia (2009-2019)

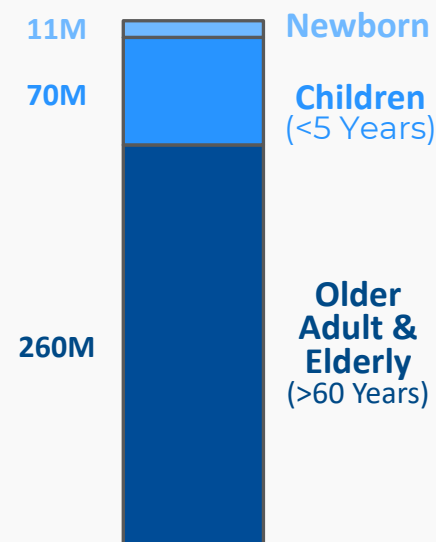


% of All Viral Acute Respiratory Infections (ARIs) (2009-2019)



## Potential Blockbuster Market in China & Globally

>340 Million Addressable Population in China <sup>(2)</sup>



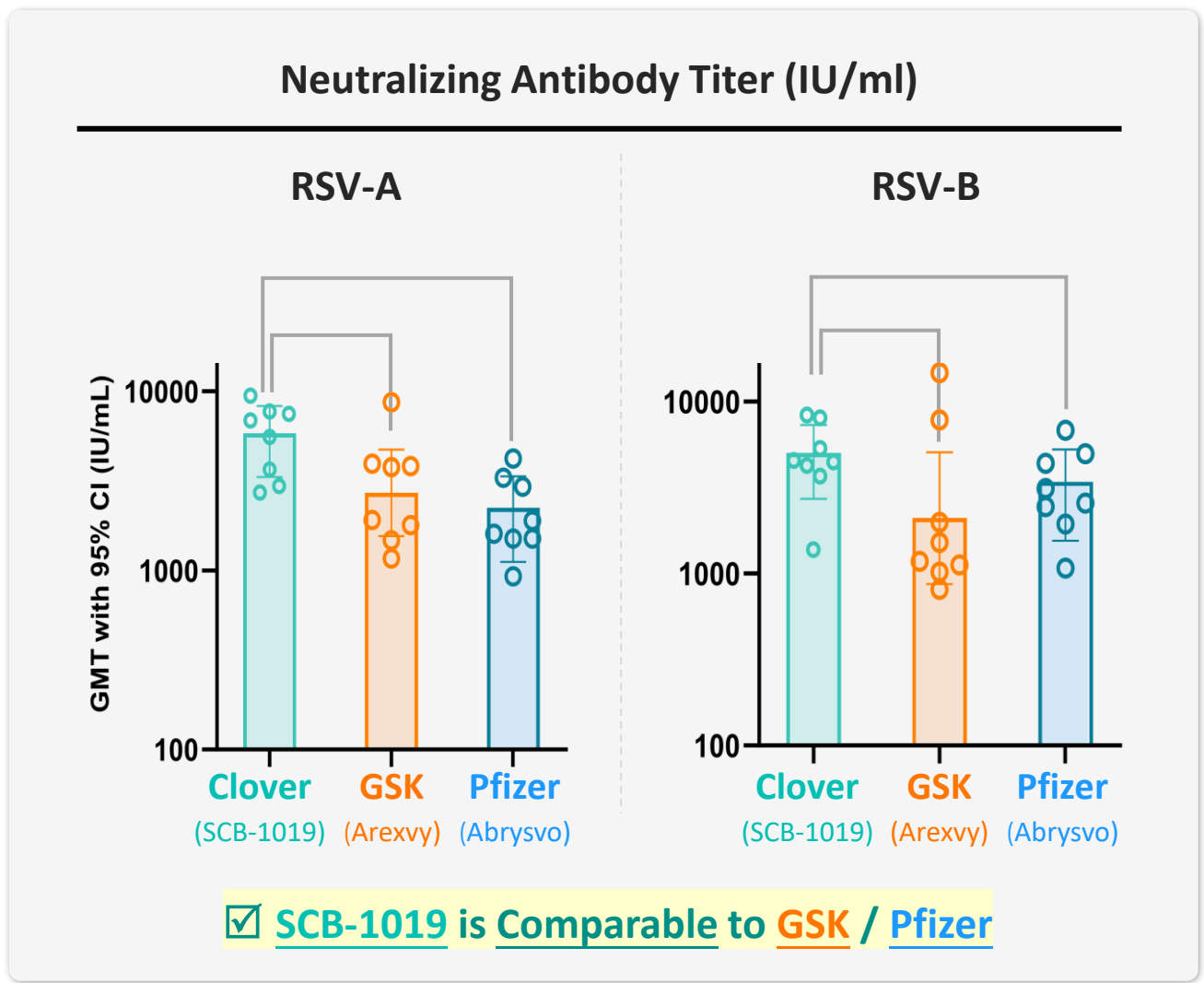
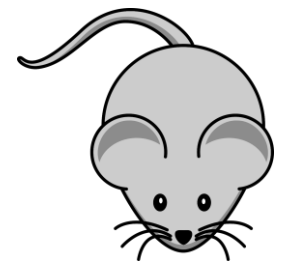
**RMB 15Bn+**  
China Potential Peak RSV Vaccine Sales <sup>(3)</sup>

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

<sup>(1)</sup> Li et al., *Nat. Commun.*, 2021 (DOI: 10.1038/s41467-021-25120-6). <sup>(2)</sup> China demographics in 2021. <sup>(3)</sup> 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]). <sup>(4)</sup> Wall Street research estimates for global older adult RSV vaccine market, including *Cowen Research* – US\$13Bn (Feb 2023), *Jefferies* – US\$15Bn (Jul 2023).

# 1

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

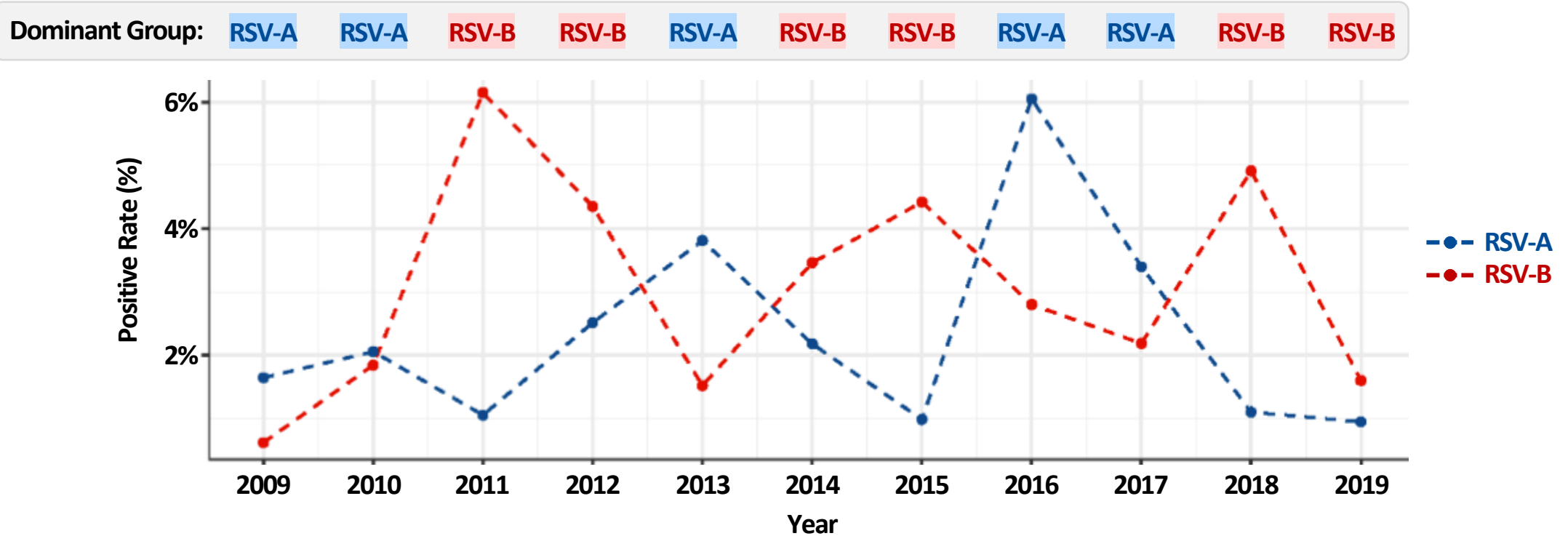


Note: Clover preclinical studies. Head-to-head comparison of SCB-1019 versus commercially-procured Arexvy (GSK) and Abrysvo (Pfizer) in primed mouse model. Mice were primed with live RSV-A virus, and after approximately 3 months, mice were given a single dose of vaccine (Day 0). Sera were collected on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

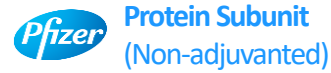
% of Acute Respiratory Viral Infections (ARIs) in China (2009-2019)



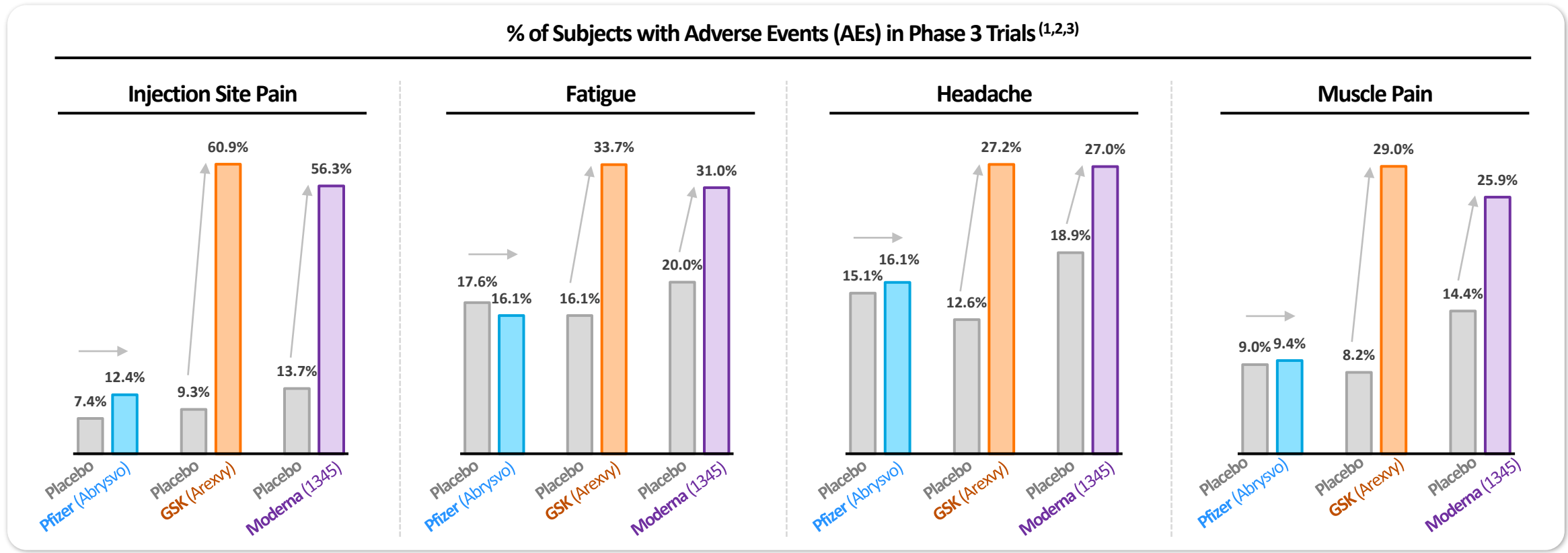
Note: Viral composition tested in 110,058 patients with ARIs in the mainland of China from 2009–2019.  
Source: Li et al., Nature Communications, 2021 (DOI: 10.1038/s41467-021-25120-6).

# 3 Differentiation in Safety & Tolerability

- Potential significant **differentiation in safety & tolerability profiles** among RSV vaccines observed in clinical trials
- **Important consideration for vaccine uptake**, especially for targeted populations (elderly & pediatrics) in China



% of Subjects with Adverse Events (AEs) in Phase 3 Trials <sup>(1,2,3)</sup>



Note: Percentage of subjects experiencing selected adverse events (AEs) following vaccination with RSV vaccine or placebo.

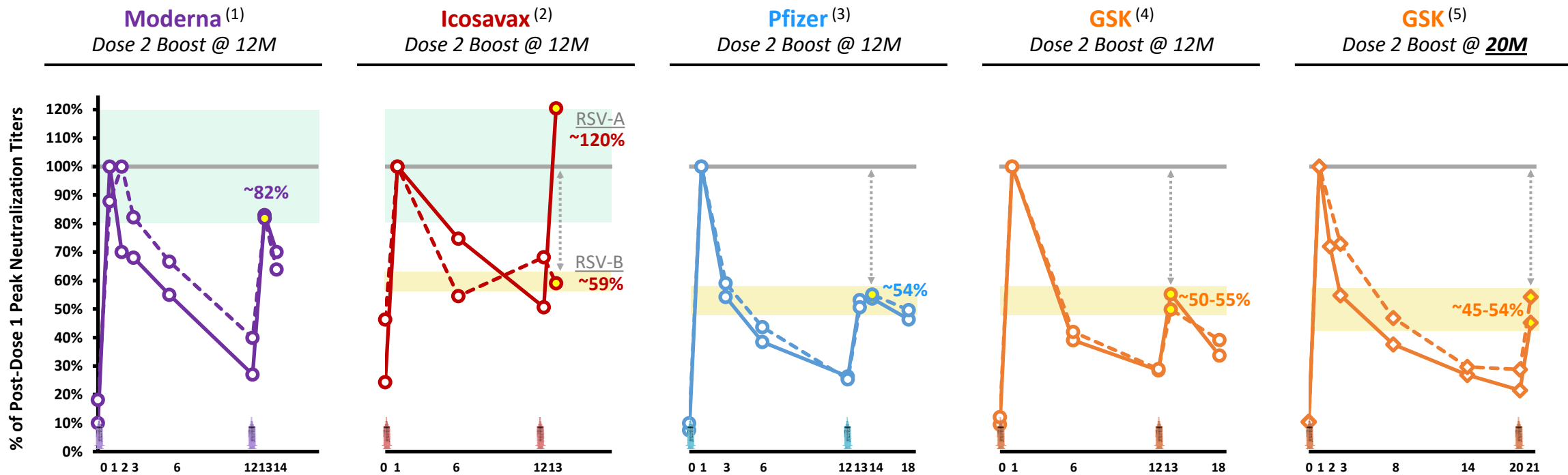
- (1) Pfizer June 2023 ACIP presentation.
- (2) GSK June 2023 ACIP presentation, NCT04732871.
- (3) Moderna 4<sup>th</sup> Vaccines Day presentation (April 11, 2023).

# 4 Potential Booster Issue for Vaccines Using T4-Foldon Tag (GSK/Pfizer)

- Neutralization Titers Only Reach ~50% of Peak Levels Following Pfizer and GSK Booster Doses in Year 2, Potentially Due to Immune-Interference from T4-Foldon Trimerization Tag Utilized by Both Vaccines
- Moderna and Icosavax Demonstrate that RSV Neutralization is Boostable in Year 2, Although Icosavax Fails to Boost RSV-B Neutralization (non-adjuvanted monovalent RSV-A vaccine)

% of Peak Neutralization Titers Post-Dose 1 <sup>(1)</sup>

—○— RSV-A Neutralization  
 - -○- - RSV-B Neutralization

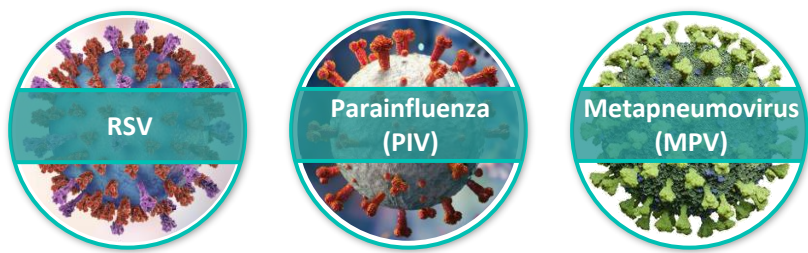


Note: Moderna, Icosavax and Pfizer neutralization titers based on IU/mL. GSK units expressed as ED<sub>60</sub>.  
 (1) Moderna ACIP Presentation (29-FEB-2024), (2) Icosavax Company Presentation IVX-121 (28-JUN-2023), (3) Pfizer 2023 VRBPAC Company Briefing Document, (4) DOI: 10.1093/infdis/jiad321. (5) GSK ACIP Presentation (21-JUN-2023).

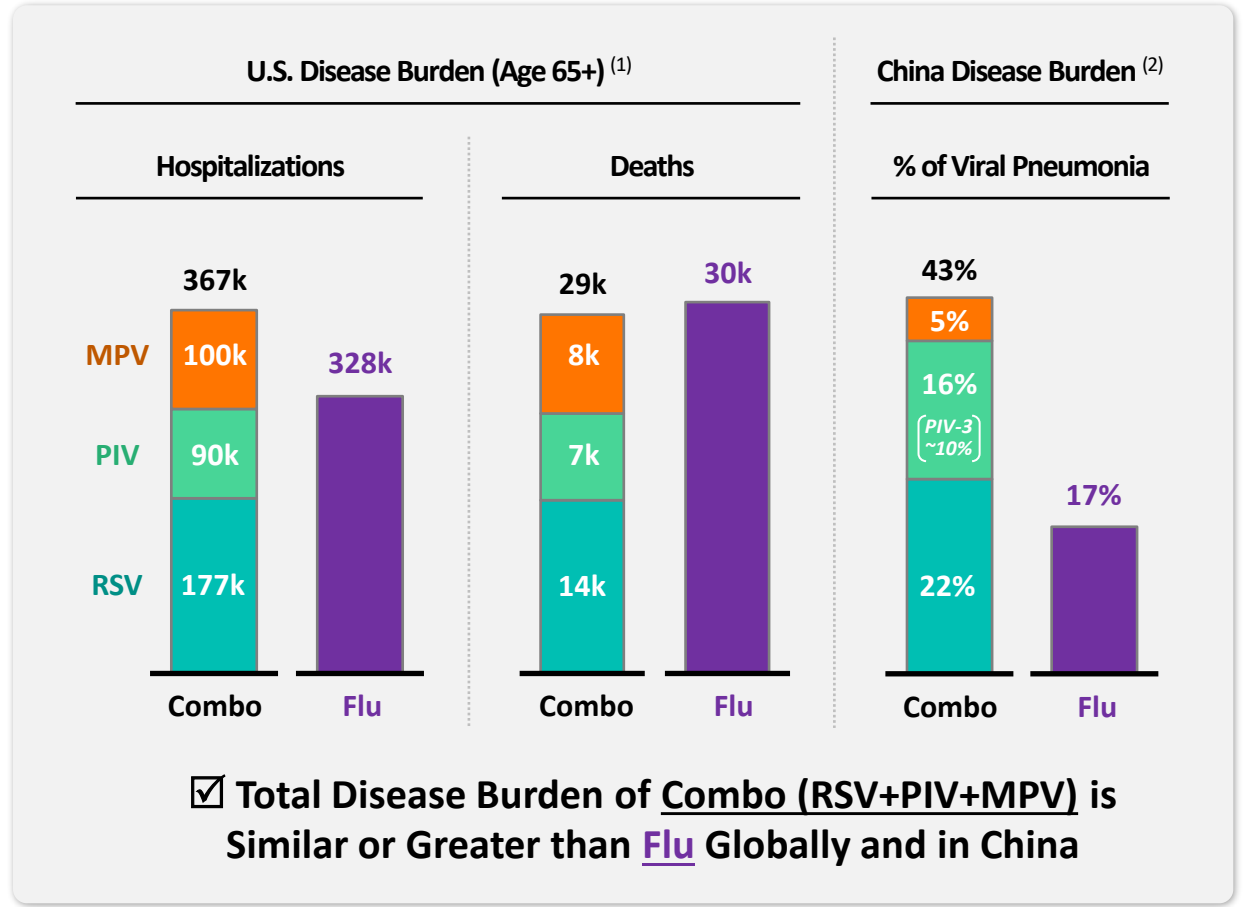


# 5 Potential for Respiratory Combo Vaccine (RSV + PIV + MPV) LCM Opportunity

- 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)
- Trimer-Tag protein subunit has platform advantages for combo versus mRNA (combo dose is limited by safety) and VLPs (complicated CMC)



- Virus Order/ Disease**
  - ✓ All 3 are Part of Mononegavirales Order
  - ✓ All 3 Cause Symptomatic Respiratory Disease
- Antigen**
  - ✓ All 3 have Similar Trimeric Fusion (F) Antigen, Requiring Stabilization in Prefusion form (PreF)
- Seasonality**
  - ✓ All 3 Observe Peak Outbreaks in Winter
- At-Risk Populations**
  - ✓ Highest Risk is Elderly and Infants/Toddlers



(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 proxy. [E] <https://www.cdc.gov/rsv/research/us-surveillance.html> [F] Compiled 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.

**Thank You!**