



**Differentiated & Potential Best-in-Class Bivalent RSV Vaccine Candidate (SCB-1019):** *Program Overview & Data Update* 

## **06 December 2024**

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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



BIOPHARMACEUTICALS

Note: Preliminary Considerations for Discussion Purposes Only. Estimated Relative Market Sizes Based on Estimates Shown for Illustrative Purposes Only and may Not be to Scale. (1) GSK and Pfizer Q3 2023, FY 2023 and Q1 2024 financial results announcements.

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

Monthly Vaccine Efficacy Point Estimates (RSV LRTD ≥2 Symptoms)<sup>(1,2)</sup>



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).

- (2) 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



#### **GSK (AREXVY) / Pfizer (ABRYSVO)**

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

**<u>Clover's Trimer-Tag</u> (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 ED<sub>60</sub>.

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).



5

<u>SCB-1019</u> has a <u>De-Risked & Potential Best-in-Class</u> 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>)



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



Note: (1) GSK June 2023 ACIP presentation, NCT04732871. Icosavax Investor Update Presentation (08-AUG-2023)

# Clover SCB-1019: Phase 1 Results in Older Adults Head-to-Head Versus GSK (AREXVY)



# Clover SCB-1019 Phase 1: Study Design

- **70 Older Adult Subjects (Age 60-85)** Enrolled to Receive Non-Adjuvanted SCB-1019, AS01<sub>E</sub>-Adjuvanted AREXVY, or Placebo
- Study Follows Previously Announced Positive Phase 1 Safety & Immunogenicity Results for SCB-1019 in 48 Older Adult Subjects



✓ 1<sup>st</sup> Clinical Trial Results Announced Globally Evaluating Head-to-Head Comparison with a Licensed RSV Vaccine (Market-Leading AS01<sub>E</sub>-Adjuvanted AREXVY Represents High Bar)



# **Clover SCB-1019 Phase 1:** *Immunogenicity Results*

RSV Neutralizing Antibody Titers for <u>Clover's Non-Adjuvanted SCB-1019</u> Matched <u>GSK's AS01-Adjuvanted AREXVY</u> 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



#### **RSV-B Neutralization Titers** (IU/mL) **Head-to-Head Comparison** Non Head-to-Head Comparisons Clover (SCB-1019) GSK (AREXVY) Moderna (MRESVIA) AZ / Icosavax (IVX-A12) Non-Adjuvanted <u>ASO1-Adjuvanteo</u> mRNA Non-Adjuvanted +2x +7x +8x +2x +6x +4x 37.684 32,022 10,000 8,203 7,457 5,500 4,986 4,639 ~4,200 3.598 ~2,000 1,353 1,300 1,000 D0 D28 D0 D28 D0 D28 D0 D28 D0 D28 Placebo D28 Vaccine: Bivalent (A/B) **RSV-A RSV-A** RSV-A (+hMPV) Phase 1 Phase 3 Phase 3 Phase 1 Phase 2 Phase: 60-85 Years 65-79 Years 60-69 Years 60-75 Years 60-85 Years Population: **Reference:** Clover Phase 1 Trial (Head-to-Head) [5] [5] [3] [4]

### ✓ 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 <u>NIBSC 16/284</u> reference sera (testing was conducted at different laboratories across clinical trials). Bars represent GMTs (± 95% confidence intervals). Abbreviations: IU/mL (International Units Per Milliliter), GMT (Geometric Mean Titer), GMFR (Geometric Mean Fold Rise). [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, [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, [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) <sup>(1)</sup>
- 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 <u>~1.5x</u> 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-1019T 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*





# **RSV Re-Vaccination:** New Insights & RSV Pre-F Construct Differentiation



#### **GSK (AREXVY) / Pfizer (ABRYSVO)**

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

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



Note: Cross Trial Comparisons for Illustrative Purposes Only. Pfizer neutralization titers based on IU/mL. GSK units expressed as ED<sub>60</sub>.

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).,



## **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

**Patent Pre-F** Mutation **Clover's SCB-1019 Utilizes a Differentiated Approach** S190I D486S 5 3 T103C 1148C  $\mathbf{V}$  $\mathbf{T}$ In-House to Producing & Stabilizing RSV PreF-Trimer S P T4 Developed F2 P27 F1 Ρηzei Foldon **Proprietary IP** S155C S190F V207L S290C **In-house Developed Proprietary Stabilizing Mutations:**  $\mathbf{\nabla}$  $\mathbf{\nabla}$  $\mathbf{T}$ Differentiated mutation approach compared to other S P **US NIH IP** F2 P27 F1 Foldon (DS-Cav1) companies and National Institute of Health (NIH); Clover focused on minimizing number of mutations in 145 A149C S155C S190F V207L S290C L373R Y458C 524 549 103 a single region to preserve native-like Pre-F structure • V  $\mathbf{T}$ **•** • **US NIH IP** S P moderna F1 ΤМ GS (Cav2) +N67I 109 137 S215P E487Q 513 Trimer-Tag: Trimer-Tag (derived from human In-House  $\mathbf{\nabla}$ S P **T4** procollagen) forms a flexible structure, enabling Developed Johnson Johnson F2 GSGSGR F1 Foldor **Proprietary IP** preservation of native-like trimeric Pre-F structure; potentially superior to T4 Foldon **V** Disulfide Bond Cavity Filling (Cav) Trimer-Interface (Acidic Patch) PreF Stabilization Strategies: P27 Deletion 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 <sup>(3)</sup>, whereas PostF does not <sup>(1)</sup>
- Stabilized <u>PreF</u> vaccines have demonstrated vaccine efficacy (GSK, Pfizer, Moderna), whereas <u>PostF</u> failed in previous clinical trials <sup>(2)</sup>







Note: NAb (Neutralizing Antibody).

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

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

(3) 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<sub>D</sub> (Dissociation Constant) measured by ForteBio assay.



# SCB-1019 Induces Differentiated 'Antibody Quality' in Mice



Antibody Quality: Neutralizing Antibody / Binding Antibody (Ratio)



### **☑** <u>SCB-1019</u> Significantly Higher

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.



#### SCB-1019 Induces Potentially Differentiated "<u>Antibody Quality</u>" in Humans

- Phase 1 Results: Group-level (n=30/group) trends observed for SCB-1019 inducing a potentially higher ratio of RSV neutralizing antibodies (NAb) to binding antibodies (ELISA) compared to GSK (AREXVY)
- Similar results were observed in Clover's in vivo preclinical studies (mice)
- 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, result could potentially confirm that Clover's Trimer-Tagged & stabilized PreF is superior to GSK/Pfizer's T4-Foldon Tagged PreF Constructs

# Ratio of Neutralizing Antibodies / ELISA Binding Antibodies<sup>(1)</sup> GMR: +1.4x 0.20 0.14 **GSK AREXVY** SCB-1019 Non-Adjuvanted AS01-Adjuvanted (N=30) (N=30)

Note: Bars represent GMFRs for Day 28 versus Day 0 (± standard error).

Preliminary results shown for validated RSV neutralizing antibody assay and exploratory ELISA assay. Abbreviations: GMFR (Geometric Mean Fold Rise), GMR (Geometric Mean Ratio), NAb (Neutralizing Antibody). (1) Calculated by dividing RSV-A neutralizing antibody titers (IU/mL) by RSV PreF-protein binding antibody ELISA titers (EC<sub>50</sub>). Bars represent GMTs (± standard error).



## Summary of <u>RSV Re-Vaccination</u> Data & <u>Clover's Potential Differentiation</u>

<u>GSK/Pfizer's Re-Vaccination</u> Results at 1- and 2-Year Intervals Have been <u>Unsuccessful to-Date</u>	<ul> <li>Both GSK/Pfizer's RSV PreF utilize <u>T4-Foldon Trimerization Tag</u> + <u>Cavity Filling Mutations</u> (with p27 preserved)</li> <li><u>T4-Foldon</u> (bacteriophage derived) reported to induce <u>'off-target' immune responses in humans</u> and <u>may destabilize PreF</u> <sup>(1)</sup></li> </ul>
<u>Clover's SCB-1019</u> Preclinical & Clinical Results To-Date Demonstrate a <u>Differentiated</u> <u>RSV PreF Construct</u>	<ul> <li><u>Clover's Trimer-Tagged RSV PreF (SCB-1019) is Differentiated &amp; Potentially More 'Native-Like' than GSK &amp; Pfizer</u></li> <li><u>In Vitro mAb Binding</u>: Differentiated &amp; higher binding affinity than GSK (AREXVY) against mAbs at highly potent PreF NAb sites (V, III)</li> <li><u>Mouse NAb-to-Binding Antibody Ratio</u>: Significantly higher ratios of NAb-to-Binding Antibodies observed for SCB-1019 versus GSK/Pfizer</li> <li><u>Phase 1 NAb-to-Binding Antibody Ratio</u>: 1.4x higher trend observed for SCB-1019 versus GSK in Phase 1 in vaccine-naïve older adults</li> <li><u>Trimer-Tag is Immuno-Silent in Humans</u>: Dosed in &gt;15,000 subjects with Trimer-Tagged COVID-19 vaccine SCB-2019 (CpG 1018/alum), with no humoral or cellular anti-Trimer-Tag responses observed</li> </ul>
<u>Working Hypothesis</u> for GSK/Pfizer's Re-Vaccination Challenges & Clover's Planned Next Steps	<ul> <li><u>GSK/Pfizer's T4-foldon tagged RSV PreF constructs</u> may be <u>non-native and/or unstable in vivo</u>, exposing <u>non-native, non-neutralizing</u> <u>antibody epitopes on RSV PreF</u> (as well as off-target T4-foldon epitopes), which are immunologically <u>primed by Dose 1</u></li> <li>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)</li> <li>Potential to overcome GSK/Pfizer's current re-vaccination challenges utilizing a heterologous re-vaccination (Dose 2) with Clover's differentiated &amp; potentially more 'native-like' Trimer-Tagged RSV PreF vaccine candidate SCB-1019</li> <li>To be further evaluated in <u>Clover's Re-Vaccination Clinical Trial for SCB-1019 (Head-to-Head vs AREXVY) Planned to Initiate in 2025</u></li> </ul>



# RSV Combination Vaccine Development (RSV + hMPV ± PIV3)



# Potential for <u>Respiratory Combo Vaccine</u> (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
- Directly leveraging Clover's RSV experience to develop 'Respiratory Combo Vaccines' across mononegavirales order of viruses (RSV + hMPV ± PIV3)
- Trimer-Tag protein subunit has platform advantages for combo versus <u>mRNA</u> (combo dose is limited by safety) and <u>VLPs</u> (complicated CMC)





✓ Total Disease Burden of <u>Combo (RSV+hMPV+PIV3)</u> is Similar or Greater than <u>Flu</u> Globally and in China

 <u>Sources</u>: [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.



# 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**

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





# **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" Ineutralizing responses); does not induce ADA/pre-existing immunity issue (enables repeated boosting & positive safety profile)
- Validated technology

logy Platform has been fully validated by COVID-19 vaccine (SCB-2019) that is authorized for Emergency Use in China



#### Strong Neutralizing Immune Responses

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



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

\* A "trimer" refers to a molecule or an anion formed by combination or association of three molecules or ions of the same substance. Trimerization is a chemical reaction that uses three identical molecules to produce a single trimer. Proteins that are created through the joining of two or more genes that originally coded for separate proteins and consist of three identical simpler parts are referred to as "trimeric fusion proteins". Trimerization tag refers to a protein tag from the C-propeptide domain of procollagen (Trimer-Tag), which is capable of self-assembly into a disulfide bond-linked trimer. (1) SARS-CoV-2 pseudovirus neutralizing antibody responses in mice vaccinated with two doses of S-Trimer (Trimer-Tagged SARS-CoV-2 spike protein) or S-Dimer (Fc-Tagged SARS-CoV-2 psike 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

## Sextensive Clinical Experience Globally

- **☑** 37,500+ Participants Enrolled Across Trials in 8 Countries
- Experience in Broad Population Groups (Elderly, Adult, Adolescent, Co-Morbidities<sup>(1)</sup>), 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.

### Sendorsed 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 ~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 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</p>



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

- Note: Cross Trial Comparisons for Illustrative Purposes Only. Moderna, Icosavax and Pfizer neutralization titers based on IU/mL, GSK units expressed as ED<sub>so</sub>
- 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)</p>
- Re-Vaccination for all RSV Vaccines is Needed (Similar to Flu & COVID-19), Potentially Every ~2 Years for Protein-Based RSV Vaccines (GSK/Pfizer)



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 Presentation), 08 OCT 2024 GSK Press Release.

- Severe RSV Endpoints:
   Primary Endpoints:
  - S: GSK (RSV-LRTD ≥2 Symptoms/Signs for ≥24 Hours), Pfizer (RSV-LRTI ≥2 Symptoms/Signs), Moderna (RSV-LRTD ≥2 Symptoms).
- Linear Regression (Severe RSV Disease):
   Linear Regression (VE Primary Endpoints):
- GSK (Y = -0.0119x + 1.0142) | Pfizer (Y = -0.0204x + 0.8115) | Moderna (Y = -0.0219x + 0.8553) GSK (Y = -0.0086x + 0.8883) | Pfizer (Y = -0.008x + 0.7155) | Moderna (Y = -0.0212x + 0.8535)
  - <u>y Endpoints)</u>: GSK (Y = -0.0086x + 0.8883) | Pfizer (Y = -0.008x + 0.7155) | Moderna (Y = -0.0212x glass of lines: for only 1 access displayed to date. Completing of the only 1 access displayed to date.
- (5) Pfizer data for cumulative vaccine efficacy for only 1 season disclosed to-date. Cumulative vaccine efficacy through mid-season 2 with 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).

✓ Efficacy for <u>Protein-Based RSV Vaccines</u>
 Appears Durable and
 Superior to <u>mRNA</u>, with
 Potential Re-Vaccination
 Interval of ~2 Years



## Elderly RSV Vaccine Phase 3 Efficacy Durability: Summary Reference Data

Vaccine Efficacy Against <u>'Severe' RSV Disease</u> (1)																		
	<b>GSK (AREXVY)</b> RSV-LRTD ≥2 Signs or 'Severe' Assessment by PI							<b>Pfi</b> RSV-LRT	<b>zer (ABRYS\</b> I ≥3 Symptol	<b>/O)</b> ms/Signs		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	30.6 Months	7.1 Months		12.0 Months	13.9 Months	16.4 Months	3.7 Months		8. Mor	6 1ths	12.0 Months	18.8 Months	
Vaccine Efficacy (95% Cl)	<b>94.1%</b> (62.4 – 99.9)		<b>84.6%</b> (56.4 – 96.1)	<b>78.8%</b> (52.6 – 92.0)	<b>74.9%</b> (48.4 - 89.2)	<b>67.4%</b> (42.4 – 82.7)	<b>85.7%</b> (32.0 - 98.7)	<b>88.9%</b> ()	<b>86.0%</b> (63.0 - 96.0)	~84% <sup>(3)</sup> ()	<b>81.5%</b> (48.2 - 80.0)	<b>82.4%</b> (34.8 - 95.3)	<b>80.9%</b> (50.1 - 92.7)	<b>63.0%</b> (37.3 - 78.2)	<b>61.1%</b> (34.7 - 76.8)	<b>55.0%</b> (31.0 - 71.0)	<b>49.9%</b> (27.8 - 65.6)	
Cases: Vaccine	<b>1</b> (12,466 Subj.)		<b>4</b> (12,469 Subj.)	<b>7</b> (12,469 Subj.)	<b>9</b> (12,468 Subj.)	<b>15</b> (12,468 Subj.)	<b>2</b> (16,466 Subj.)	<b>2</b> (~18,000 Subj.)		<b>5</b> (~10,000 Subj.)	<b>10</b> ()	<b>3</b> (17,572 Subj.)	<b>5</b> (17,561 Subj.)	<b>19</b> (18,112 Subj.)	<b>20</b> (18,074 Subj.)		<b>46</b> (18,181 Subj.)	
Cases: Placebo	<b>17</b> (12,494 Subj.)		<b>33</b> (12,498 Subj.)	<b>48</b> (12,498 Subj.)	<b>54</b> (12,498 Subj.)	<b>75</b> (12,498 Subj.)	<b>14</b> (16,308 Subj.)	<b>18</b> (~18,000 Subj.)		<b>32</b> (~10,000 Subj.)	<b>54</b> ()	<b>17</b> (17,516 Subj.)	<b>26</b> (17,503 Subj.)	<b>51</b> (18,045 Subj.)	<b>51</b> (18,010 Subj)		<b>91</b> (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 <u>'Moderate-to-Severe' RSV Disease</u><sup>(2)</sup>

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

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(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).

(3) 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!**

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