Innovation to drive sustainable growth in Vaccines

Part 1

Vaccines Investor Event
June 29, 2023
Forward-looking statements

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Agenda

Vaccines Investor Event, June 29, 2023

2:00-2:10  Introduction

2:10-3:00  Expand leadership
- Deliver Best-in-Class RSV franchise
- Win in Influenza

3:00-3:20  Q&A

3:20-3:40  Break

3:40-4:30  New growth areas in vaccines
- Enter multi-billion PCV market
- Establish Best-in-Class meningitis portfolio
- Leverage leading-edge mRNA platform
- New frontiers

4:30-4:40  Concluding remarks

4:40-5:00  Q&A
Introduction

Paul Hudson
Chief Executive Officer
Driving *growth* with strategic choices

**Dupixent®**
Maximize patient benefits with ambition to achieve >€13bn peak sales across type 2 inflammatory diseases [COPD not included]

**Vaccines**
Expected mid-to-high single-digit growth\(^1\), through differentiated products, market expansion, launches

**Pipeline**
Prioritize and accelerate portfolio of potentially transformative therapies

- **€8.3bn** sales in 2022, +43.8% 5 years after launch
- **6.3%** growth in 2022
- **84** projects in clinical development

\(^1\) Sales CAGR from 2018 base to 2025
**Strategic transformation** delivered first set of guidance targets

**2020 - 2022**

- 10 consecutive quarters of **growth**
- 540bps **BOI margin improvement** from 2019 to 2022¹
- **€2.7bn cost savings** re-invested in growth drivers
- >25 **value-creating** BD and M&A deals
- Accelerating **digitalization**: use of AI and data science at scale

**Strong cash flow**

- **BOI margin** 30%

**Ahead of guidance**

- **EPS growth** ~16% growth at CER

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¹ 2018 proforma BOI margin of 24.6% without equity investment in Regeneron sold in May 2020, excluding IFRS16 impacts.
Powerful business and pipeline momentum in 2023

**Launches**

- ALTUVIIIO™
- Beyfortus® (nirsevimab)
- Tzield™ (teplizumab-mzwv)

**Pivotal readouts**

- Dupixent™ (dupilumab)
  - Expansion into COPD
- Tolebrutinib (BTKi)
  - Relapsing MS
- Fitusiran
  - Hemophilia A/B

**Early to mid-stage pipeline**

- **27 readouts** in immunology, vaccines, neurology, rare diseases, and oncology

Baring unforeseen events.
Strong *positive* pipeline news flow in H1 2023

<table>
<thead>
<tr>
<th>Submissions</th>
<th>Dupixent®</th>
<th>CSU</th>
<th>US</th>
<th>300,000 people with CSU inadequately controlled by antihistamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read-outs</td>
<td>Dupixent®</td>
<td>COPD</td>
<td>Phase 3</td>
<td>Around 900,000 patients in G7</td>
</tr>
<tr>
<td></td>
<td>itepekimab (IL-33)</td>
<td>COPD</td>
<td>Phase 3 IA</td>
<td>Around 1.8m patients in G7</td>
</tr>
<tr>
<td></td>
<td>amlitelimab (OX40L)</td>
<td>AD</td>
<td>Phase 2b</td>
<td>Moving in phase 3</td>
</tr>
<tr>
<td></td>
<td>frexalimab (CD40L)</td>
<td>MS</td>
<td>Phase 2b</td>
<td>Moving in phase 3</td>
</tr>
<tr>
<td></td>
<td>SAR’765 (IL-13/TSLP)</td>
<td>Asthma</td>
<td>Phase 1b</td>
<td>Moving in phase 2b</td>
</tr>
<tr>
<td></td>
<td>SAR’566 (oral TNFi)</td>
<td>Psoriasis</td>
<td>Phase 1b</td>
<td>Moving in phase 2b</td>
</tr>
</tbody>
</table>

Barring unforeseen events. Dupixent is not yet approved neither in CSU nor COPD by any regulatory authority; itepekimab, amlitelimab, frexalimab, SAR’765 and SAR’566 are still under investigation and not yet approved.
**Play to Win:** Leverage innovation to drive *next growth chapter*

**2020-2022**
- Refocus with decisive actions
- Growth through winning assets
- Margin expansion

**2023-2025**
- Transformative launches
- Agile and efficient resource deployment
- Leading R&D productivity

**2026-2030**
- Industry leader in immunology with >€22bn sales by 2030
- Doubling vaccines sales by 2030\(^1\)
- No meaningful LOE
- Ambition to launch 3-5 new products with €2-5bn peak sales potential each

Barring unforeseen events. 1. Sales from 2018.
Expand leadership in vaccines

Thomas Triomphe
Head of Vaccines GBU

Jean-François Toussaint
Head of Vaccines R&D
Our ambition in **Vaccines**

- Continued strong growth driven by four core franchises: Influenza, Meningitis, PPH & Boosters, RSV
- Unlock the potential of mRNA in Vaccines with Next-Generation platform
- Build an industry leading pipeline to address unmet needs

*More than double Vaccine sales by 2030*

1. Vs. 2018, risk adjusted, internal estimate
Execution of *Play To Win* strategy in Vaccines

**Focus on growth**
+8% Sales growth 2018-2022 CAGR
2 Vaccines reached blockbuster status
  - Fluzone HD
  - Penta/Hexaxim

**Lead with innovation**
32 Countries with Beyfortus licenses
6 New phase 1/2 programs over 2022-2023

**Accelerate efficiency**
+6pts Vaccines profitability from 2018 to 2022
1 Merged Pharma & Vaccines manufacturing & supply, 2 Evolutive Facilities on track for 2025 operation

**Reinvent how we work**
+90% TBio experts retained across mRNA Center of Excellence 2 years post-acquisition
45% Female senior leaders
R&D transformation has started to deliver strong results

State-of-the-art immunology & antigen design
- Innovative antigens designed, including mRNA-encoded bacterial vaccine approach
- High throughput translational science & proprietary MIMIC® technology introduced

Selecting the best technology platform for each target
- 9 vaccine technologies employed across the pipeline
- Leading-edge mRNA platform added

Expanding into new infectious diseases
- Chlamydia final antigens selected
- Acne mechanism of action validated
- Additional new research programs initiated

* Compared to Dec 2021
At least 5 new FiC / BiC programs expected to enter phase 3 by 2025

2022-2023 progress

3 new products registered

6 new phase 1/2 programs

- mRNA Flu QIV
- RSV Older Adult
- RSV OA/PIV/hMPV
- MenPenta
- Acne
- NextGen Flu

Pipeline moving at pace
Recent highlights from our *leading-edge mRNA platform*

**AI/ML augmented mRNA Workforce**
- >600 experts and more than 30 collaborations across all aspects of the platform
- Proprietary generative modeling for mRNA and lipid design

**Next generation mRNA products**
- As many as 5 distinct LNPs clinically tested by 2023
- 4 mRNA enhancement features for next clinical candidate

**Rapid deployment across the pipeline**
- Pivot to modified mRNA and clinical validation in 9 months
- 7 phase 1/2 launched since 2022
Sanofi Vaccines is built on strong foundations

**R&D toolbox**
9 vaccine technologies employed across the pipeline

**Industrial powerhouse**
Ability to deliver at scale

**Extensive medical expertise**
Innovative approaches to generate impactful real-world evidence

**Commercial strength**
Engagement of strong stakeholder networks

We have what it takes to win in protection against preventable diseases
Sanofi *societal commitments* embedded in our business

**Affordable access**
Ensuring access to medicines for the poorest countries

**R&D for unmet needs**
Acting for the most vulnerable communities

**Planet care**
Building sustainability for a healthy planet

**In and beyond the workplace**
Building an inclusive workplace

- Yellow Fever vaccine
- Blister-free vaccine
Yellow Fever program with thorough *Global Access Plan*

- **109,000 severe infections** and **51,000 deaths** in 2018 worldwide

- **>500 million doses** distributed worldwide since 1953

  Major partner and supplier of UNICEF, committed to stay ready to respond to outbreaks

- **Positive phase 2 results** of our next generation vaccine
Ambition to manufacture 100% **blister-free packaging** by 2027

- Saving ~330 tons of plastic per year
  Reducing the amount of microplastics in the environment

- Up to 50% reduction of transported pallets
  Reducing the need for cold chain space and transport by ~1/3rd

- 30% reduction in distribution costs

- 40% of blister-free syringes by end of 2023, **100% by 2027**
**New data** from 12 assets featured today

<table>
<thead>
<tr>
<th>Deepen our leadership in existing franchises</th>
<th>New growth areas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza</strong></td>
<td><strong>Pneumo</strong></td>
</tr>
<tr>
<td>Fluzone HD</td>
<td>PCV21</td>
</tr>
<tr>
<td>Influenza QIV mRNA</td>
<td></td>
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<tr>
<td>Next-gen mRNA Flu vaccine</td>
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<tr>
<td><strong>Meningitis Travel &amp; Endemic</strong></td>
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<tr>
<td>MenQuadfi</td>
<td></td>
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<tr>
<td>MenB</td>
<td></td>
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<tr>
<td>MenPenta</td>
<td></td>
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<tr>
<td>Next-gen</td>
<td></td>
</tr>
<tr>
<td>Yellow fever</td>
<td></td>
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<tr>
<td>Next-gen rabies</td>
<td></td>
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<tr>
<td><strong>RSV</strong></td>
<td></td>
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<tr>
<td>Beyfortus</td>
<td></td>
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<tr>
<td>RSV toddler</td>
<td></td>
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<tr>
<td>RSV older adult (OA)</td>
<td></td>
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<tr>
<td>RSV OA respiratory combo</td>
<td></td>
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<tr>
<td><strong>New frontiers</strong></td>
<td></td>
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<tr>
<td>Chlamydia</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td></td>
</tr>
</tbody>
</table>

Fluzone HD pediatric
Pandemic Influenza

Data to be shared today
Deliver Best-in-Class RSV franchise

Kimberly Tutwiler
Head of RSV Franchise

Jean-François Toussaint
Head of Vaccines R&D
Ambition to **lead in RSV** across all target populations

**RSV Market**

- **Infant**
  - 30%
- **Toddler**
  - 10%
- **Older Adult**
  - 60%

- **RSV Market**
  - ~€8bn
  - 2030

**Beyfortus**
Best-in-Class immunization for All Infant Protection in first season

**RSV Toddler**
SP0125: First-in-Class vaccine for protection from second season onwards

**RSV Older Adult**
SP0256: First-in-Class RSV-hMPV-PIV combination

Source: Sanofi internal forecast
U.S. Advisory committee votes **21-0** in favor of nirsevimab

**Unanimously voted in favor for 1st season**
- Favorable benefit/risk profile for prevention of RSV LRTD in newborns & infants born during or entering 1st season

**Voted 19-2 in favor for 2nd season**
- Favorable benefit/risk profile for prevention of RSV LRTD in children up to 24 months of age who remain vulnerable

**ACIP meeting anticipated before the RSV season**
**HARMONIE** study confirms pivotal trial data in *real world setting*

- **Participants:** 8,000+ infants ≥29 weeks gestational age

- **Beyfortus**
  - N = 4,037

- **No intervention**
  - N=4,021

**Primary endpoint**
- Reduction of hospitalization due to RSV Lower-Respiratory-Tract-Infection (LRTI)

**Study objectives**
- Showcase seamless implementation in real world setting
- Enrich hospitalization data in France, Germany and UK
- Confirm safety profile in large population

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SB Drysdale, (2023, May 8–12). A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to respiratory syncytial virus (RSV) in infants (HARMONIE) [Oral presentation]. ESPID 2023: Lisbon, Portugal.  1. Not eligible for palivizumab
## Excellent safety and tolerability profile confirmed

### Adverse Events Table

<table>
<thead>
<tr>
<th>Adverse Events Category</th>
<th>Nirsevimab (N=4,016)</th>
<th>No Intervention (N=4,020)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any treatment emergent adverse event (TEAE)</strong></td>
<td>1,479 (36.8)</td>
<td>1,326 (33.0)</td>
</tr>
<tr>
<td>Leading to discontinuation of study</td>
<td>1 (&lt; 0.1)</td>
<td>1 (&lt; 0.1)</td>
</tr>
<tr>
<td>Leading to death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Grade 1 severity</td>
<td>1,171 (29.2)</td>
<td>1,014 (25.2)</td>
</tr>
<tr>
<td>Grade 2 severity</td>
<td>462 (11.5)</td>
<td>436 (10.8)</td>
</tr>
<tr>
<td>Grade 3 severity</td>
<td>48 (1.2)</td>
<td>46 (1.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>67 (1.7)</td>
<td>56 (1.4)</td>
</tr>
<tr>
<td><strong>Any study treatment related TEAE</strong></td>
<td>86 (2.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Leading to discontinuation of study</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Leading to death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Grade 1 severity</td>
<td>68 (1.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Grade 2 severity</td>
<td>21 (0.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Grade 3 severity</td>
<td>1 (&lt; 0.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (&lt; 0.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><strong>Any serious TEAE</strong></td>
<td>89 (2.2)</td>
<td>67 (1.7)</td>
</tr>
<tr>
<td>Leading to discontinuation of study</td>
<td>1 (&lt; 0.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Leading to death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
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SB Drysdale, (2023, May 8–12). A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to respiratory syncytial virus (RSV) in infants (HARMONIE) [Oral presentation]. ESPID 2023: Lisbon, Portugal.
Impressive 83% reduction of RSV-LRTI hospitalizations confirmed in real world setting

RSV is the leading cause of hospitalization in infants

Efficacy of Beyfortus has been consistent across all studies, and is maintained for 5 months to cover the duration of the RSV season

Nirsevimab expected to prevent 3x more RSV events than maternal vaccine

Modeled impact of nirsevimab and maternal immunization in a U.S. birth cohort for first RSV season

Key input

<table>
<thead>
<tr>
<th>nirsevimab</th>
<th>Maternal Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy RSV MA-LRTI</strong></td>
<td>79.5%</td>
</tr>
<tr>
<td><strong>Reduction of RSV MA-LRTI hospitalization</strong></td>
<td>83.2%</td>
</tr>
<tr>
<td>% reduction of RSV-related events in babies born before season</td>
<td>50.5%</td>
</tr>
<tr>
<td>% reduction of RSV-related events in babies born preterm</td>
<td>60.6%</td>
</tr>
<tr>
<td><strong>Immunization coverage rate</strong></td>
<td>80%</td>
</tr>
</tbody>
</table>

**Efficacy all-cause LRTI hospitalizations**: 58% for MA-LRTI all-cause (success criteria not met)

Source Notes:

1. Included RSV MA LRTI all cause (2.5%) in the absence of data for all cause LRTI hospitalization to compare

Investor Event
Ready to launch Beyfortus in the 2023 season

Stakeholders fully engaged

- Licensed in EU, Great Britain, Canada
- Broad population programs expected in Spain and France
- License, ACIP recommendation and VFC inclusion expected soon
- Contracting and reimbursement underway
- Priority review granted

Production is already underway

Beyfortus in the 2023 season
RSV in **toddlers**: significant burden in 2\textsuperscript{nd} season and beyond

![RSV Burden in Toddlers](image)

**High rate of GP consultations due to diseases caused by RSV** (0 to 5 years of age)

- Bronchiolitis: 16.1
- Antibiotic prescription: 6.9
- Respiratory disease: 4.4
- Acute respiratory disease: 3.7
- Pneumonia: 0.6

SP0125 is the *first RSV vaccine* designed to protect all toddlers.

Intranasal delivery design for *complete toddler protection*

- RSV inhibition at its *point of entry*
- *Broad protection* against both upper and lower respiratory tract disease

Live attenuated vaccine uniquely designed to *ensure safety* and *maximize immunogenicity*
Beyfortus and RSV Toddler vaccine provide continuous protection

First RSV Season (October – March)

Beyfortus administered ahead or during first season

Protected for first RSV season

April - September

1<sup>st</sup> dose of RSV Toddler vaccine

2<sup>nd</sup> dose of RSV Toddler vaccine

To be given during existing routine visits

Second RSV Season (October – March)

Protected from second RSV season onwards
Live attenuated vaccine (SP0125) *Phase 1/2 design*

- **Toddlers 6-18 mo**
  - Days 1
  - RSVt - Low dose: n=61
  - RSVt - High dose: n=57
  - Placebo: n=61

- **Safety**
  - Adverse events following vaccination

- **Immunogenicity**
  - Neutralizing antibody responses

- **Vaccine response rate**
  - Composite endpoint factoring immunogenicity and vaccine virus replication
SP0125 demonstrated safety profile *similar to placebo*

<table>
<thead>
<tr>
<th>Participants experiencing at least one unsolicited AE within 28 days after vaccination</th>
<th>First administration</th>
<th>Second administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RSVt LD (n=61)</td>
<td>RSVt HD (n=57)</td>
</tr>
<tr>
<td>Not related to vaccination</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Related to vaccination</td>
<td>5 (8.2)</td>
<td>6 (10.5)</td>
</tr>
<tr>
<td>AE of special interest*</td>
<td>15 (24.6)</td>
<td>8 (14.0)</td>
</tr>
<tr>
<td>Medically attended AE</td>
<td>28 (45.9)</td>
<td>23 (40.4)</td>
</tr>
<tr>
<td>AE leading to study discontinuation</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>1 (1.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* Based on investigator assessment. AE of special interest: acute otitis media, upper and lower respiratory infections.
**Strong vaccine response** observed with SP0125

* Strong (93%) vaccine response after two administrations of the High dose formulation
* Marginal difference between the Low and High dose formulations

* Absence of prior exposure to RSV was determined by measuring serum IgA before vaccination
Both formulations induced a robust immune response

Robust neutralizing antibody response in toddlers not previously exposed to RSV\(^1\)

Similar immune response observed for the Low and High dose formulations

Immune response in line with prior studies that showed reduction of RSV-medically attended disease\(^2\)

Move to phase 3 in H1 2024

\(^1\) Absence of prior exposure to RSV was determined by measuring serum IgA before vaccination. \(^2\) Karron et al. Am J Respir Crit Care Med Vol 203:5, 2021
RSV Older Adult: addressing important unmet need with the most compelling respiratory combination vaccine

Disease burden from RSV-hMPV-PIV similar to Influenza

Estimated burden in US >65 population:

<table>
<thead>
<tr>
<th></th>
<th>RSV</th>
<th>hMPV</th>
<th>PIV</th>
<th>Combo</th>
<th>Influenza</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalisations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(proportion of vaccinated flu burden)</td>
<td>177K</td>
<td>100K</td>
<td>90K</td>
<td>367K</td>
<td>280K</td>
</tr>
<tr>
<td>Deaths</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(proportion of vaccinated flu burden)</td>
<td>14K</td>
<td>8K</td>
<td>7K</td>
<td>29K</td>
<td>30K</td>
</tr>
</tbody>
</table>

Limited antigenic drift of RSV, hMPV and PIV removes need for annual vaccination

References:
SP0256 *Phase 1/2* trial design of mono vaccine in older adults

**Safety**
- Adverse events following vaccination

**Immunogenicity**
- Serum neutralizing antibody response measured by plaque reduction neutralization assay

- **Adults 18-49 & ≥60 yo**
- Dose 1: mRNA LNP #1, n = 10 & 100
- Dose 2: mRNA LNP #2, n = 10 & 100
- Dose 3: mRNA LNP #1, n = 10 & 100
- Dose 3: mRNA LNP #2, n = 10 & 100
- Placebo, n = 10 & 100
**Positive phase 1/2 results** support SP0256 as the backbone for the combo respiratory vaccine

- mRNA RSV OA vaccine was **well tolerated**
- mRNA RSV OA vaccine **significantly boosted** RSV neutralizing antibody responses

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**Reactogenicity (selected formulation)**

<table>
<thead>
<tr>
<th>% participants with solicited reactions D7</th>
<th>Vaccine Younger Adults 18-49</th>
<th>Vaccine Older Adults &gt;60</th>
<th>Saline Older Adults &gt;60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>40</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Grade 2</td>
<td>60</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Grade 3</td>
<td>80</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

**Boosted RSV-A Neutralizing Antibodies (selected formulation)**

<table>
<thead>
<tr>
<th>Neut Ab GMTR (D29/D1)*</th>
<th>Vaccine Younger Adults 18-49</th>
<th>Vaccine Older Adults &gt;60</th>
<th>Saline Older Adults &gt;60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>11.5</td>
<td>5.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Grade 2</td>
<td></td>
<td></td>
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<tr>
<td>Grade 3</td>
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</tbody>
</table>

*RSV-A neutralizing antibodies Geometric Mean Titer ratio (D29 vs baseline D1)

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38 Vaccines Investor Event
Only Sanofi has the potential to offer **Best-in-Class protection** for all targeted ages

<table>
<thead>
<tr>
<th></th>
<th><strong>Beyfortus</strong></th>
<th><strong>SP0125</strong></th>
<th><strong>SP0256</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROFILE</strong></td>
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<tr>
<td></td>
<td><strong>Best-in-Class for All Infant Protection</strong> in first season</td>
<td><strong>First-in-Class</strong> vaccine for <strong>second season</strong> onwards</td>
<td><strong>First-in-Class</strong> with <strong>RSV-hMPV-PIV mRNA</strong> combination</td>
</tr>
</tbody>
</table>
| **NEXT STEPS** | **Ready for launch** | **Phase 3 start in H1 2024**  
**Target submission in 2026** | **Phase 2b RSV & Phase 1/2 combo start in 2023**  
**Target submission for combo in 2026+** |
Win in Influenza

Bill Averbeck
Head of Influenza Franchise

Saranya Sridhar
Head of Translational Medicine
Sanofi is the *global leader in Influenza vaccines*

- *Pioneered the transition to quadrivalent flu vaccines*
- *Worldwide market leader with €3bn sales in 2022*
- *Established Protection Beyond Flu as the new standard of care*
- *Pursuing the next chapter in flu with mRNA technology*

Leading with innovation rooted in *Protection Beyond Flu*
Three attributes imperative for winning in seasonal flu

<table>
<thead>
<tr>
<th>Protection Beyond Flu</th>
<th>Demonstrated efficacy in hospitalization and infection reduction through high quality / consistent data – not just immunogenicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety &amp; tolerability</td>
<td>Excellent tolerability profile</td>
</tr>
</tbody>
</table>
| Administration         | Fully liquid formulation, pre-filled syringe  
                          Shelf life covering duration of flu season at refrigerator temperature (2-8°C)                                            |
It takes *Protection Beyond Flu* to win

Fluzone HD share of U.S. 65+ years old flu market value, $bn

Source: Sanofi internal analysis

Fluzone HD and Flublok in CDC preferential recommendation for 65+
Fluzone High-Dose/Efluelda set the bar high in 60/65+

**Outstanding results confirmed in most recent randomized real-world studies**

<table>
<thead>
<tr>
<th></th>
<th>DANFLU-1</th>
<th>DANFLU-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective</strong></td>
<td>Impact of QIV HD vs SD on pneumonia and influenza (P&amp;I) and other hospitalizations</td>
<td>Impact of QIV HD vs SD on P&amp;I and other hospitalizations</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Randomized real-world study 12k subjects 65-79</td>
<td>Randomized real-world study Target 208k subjects 65+</td>
</tr>
<tr>
<td><strong>Outcome / next steps</strong></td>
<td><strong>64.4% reduction in P&amp;I hospitalization</strong>&lt;br&gt;Presented at ESC 2022, accepted in NEJM Evidence</td>
<td>19k randomized to date&lt;br&gt;Started in 22/23 season</td>
</tr>
</tbody>
</table>

**Driving global expansion**

Recommendations or preferential reimbursement in 10+ key markets

HCPs and consumers are unlikely to use vaccines with 3x severe side effect burden compared to Standard Dose

HCPs

% Preference Share

-69%

SoC, mRNA vaccine with 2x Grade 2 side effects vs. SoC, mRNA vaccine with 3x Grade 3 side effects vs. SoC

Consumers

% Preference Share

-69%

SoC, mRNA vaccine with 2x Grade 2 side effects vs. SoC, mRNA vaccine with 3x Grade 3 side effects vs. SoC

HCPs do not accept administration hurdles for flu vaccines

Flu vaccination networks set up to maximize access; unfit to manage ultra-cold chains and short shelf life

Lack of refrigerator-stable, full-season product could decrease HCP uptake/use by -37%

Comprehensive *mRNA flu vaccine* program SP0273

**mRNA Flu QIV**

- **Adults 18-64 yo** & **Adults ≥65 yo**
- **mRNA Flu QIV Dose 1**
  - n=65 & 65
- **mRNA Flu QIV Dose 2**
  - n=65 & 65
- **mRNA Flu QIV Dose 3**
  - n=65 & 65
- **Fluzone Standard Dose**
  - n=60 & 60
- **Flublok**
  - n=60 & 60
- **Fluzone High-Dose**
  - n=0 & 60

**Phase 1/2 study**

**Flu QIV** (modified mRNA)
- Safety and immunogenicity with 3 different LNPs

**Neuraminidase** (unmodified mRNA and LNP#1)
- Pilot study to test neuraminidase immunogenicity

**mRNA neuraminidase (NA)**

- **Adults 18-64 yo** & **Adults ≥65 yo**
- **mRNA NA Dose 1**
  - n=30 & 30
- **mRNA NA Dose 2**
  - n=30 & 30
- **mRNA NA Dose 3**
  - n=30 & 30
- **Fluzone High-Dose**
  - n=30 & 30
Strong immune responses against A strains

Hemagglutination inhibition titers in 18-64 years old

- Immune response for A strains comparable to SoC
- Immune responses for B strains trend lower than SoC

SP0273 results

- Strong immune responses against A strains
- Hemagglutination inhibition titers comparable to SoC
- Immune responses for B strains trend lower than SoC

- GMTR D29/D01
- % Seroconversion

SP0273 mRNA Flu QIV  Fluzone SD  Flublok

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**Immune response in line** with other mRNA flu vaccine program

**Hemagglutination inhibition titers**

- **Sanofi** 18-64 years

- Competitor data \(^1\) >18 years

**mRNA flu QIV results**

In both mRNA trials:

- A strain results similar to comparator

- Low B response is a class effect across mRNA platforms

---

1. Moderna Third Annual Vaccines Day March 24th, 2022. Phase 2, Age group 18 y and older. DISCLAIMER: data from separate studies should be interpreted with care.
SP0273 reactogenicity compares favorably to other mRNA trial

**Reactogenicity in 18-64 years**

- Reactogenicity higher compared to current licensed flu vaccines
- Systemic reactions lower than in a comparator mRNA vaccine in a different trial

---

1. Data collected by Moderna in 18-49 years volunteers in a separate phase 2 trial. Moderna Third Annual Vaccines Day March 24th, 2022. DISCLAIMER: data from separate studies should be interpreted with care.
Ambition to match our Standard of Care in influenza with *Sanofi’s next-generation mRNA vaccine*

- **Machine learning**: Utilize advanced computational techniques to optimize strain selection
- **Antigen composition**: Focus on neuraminidase to improve vaccine effectiveness

*Protection Beyond Flu* is the centerpiece of clinical efforts
Potential to **improve coverage with Machine Learning**

Proof of concept achieved for H3 & H1 strains

ML model robustly selects strains with *greater breadth*\(^1\)

**ML-strains cover broader H1 Seasonal Influenza Space vs WHO strain\(^2\)**

ML offers meaningful advances in strain selection process *as demonstrated now also for H1 strains*

1. Theoretical representation for illustrative purposes
2. Log2 fold change of mNT titers compared to WHO strain. Color boxes represent different H1 sequence clades from Nexstrain
Comprehensive *mRNA flu vaccine* program

**SP0273**

**mRNA Flu QIV**

- **Adults 18-64 yo** & **Adults ≥65 yo**
  - mRNA Flu QIV Dose 1
  - mRNA Flu QIV Dose 2
  - mRNA Flu QIV Dose 3
  - Fluzone Standard Dose
  - Flublok
  - Fluzone High-Dose
  - n=65 & 65
  - n=60 & 60
  - n=0 & 60

**Phase 1/2 study**

*Flu QIV* (modified mRNA)
- Safety and immunogenicity with 3 different LNPs

**mRNA neuraminidase (NA)**

- **Adults 18-64 yo** & **Adults ≥65 yo**
  - mRNA NA Dose 1
  - mRNA NA Dose 2
  - mRNA NA Dose 3
  - Fluzone High-Dose
  - n=30 & 30
  - n=30 & 30
  - n=30 & 30

**Neuraminidase** (unmodified mRNA and LNP#1)
- Pilot study to test neuraminidase immunogenicity
**mRNA neuraminidase immunogenicity as strong as Fluzone HD**

### mRNA neuraminidase results

- Immune responses comparable to Fluzone HD
- **NB:** Fluzone HD has 2.5 to 3 times higher NA concentrations than SD vaccines and sets the bar for future vaccines
- Good tolerability and safety, comparable to Fluzone HD

---

2. Data on file

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**Neuraminidase inhibition titers (N2)**

2. Data on file

---

**mRNA neuraminidase results**

- Immune responses comparable to Fluzone HD
- **NB:** Fluzone HD has 2.5 to 3 times higher NA concentrations than SD vaccines and sets the bar for future vaccines
- Good tolerability and safety, comparable to Fluzone HD
Offering *superior* flu protection for key age groups at risk

**Vaxigrip Tetra / Fluzone SD**

**Flublok / Supemtek**

**Fluzone HD / Efluelda**

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**SP0273 Next-generation mRNA flu**

Enhance B strain immune response, improve immunogenicity, upgrade antigen design & optimize strain selection via machine learning

Acceptable tolerability and thermostability
Q&A session Part 1

Thomas Triomphe  
*Head of Vaccines GBU*

Jean-François Toussaint  
*Head of Vaccines R&D*

Kimberly Tutwiler  
*Head of RSV Franchise*

Bill Averbeck  
*Head of Influenza Franchise*

Saranya Sridhar  
*Head of Translational Medicine*
Innovation to drive sustainable growth in Vaccines

Part 2

Vaccines Investor Event
June 29, 2023
Agenda

Vaccines Investor Event, June 29, 2023

2:00-2:10  Introduction
2:10-3:00  Expand leadership
          - Deliver Best-in-Class RSV franchise
          - Win in Influenza
3:00-3:20  Q&A
3:20-3:40  Break
3:40-4:30  New growth areas in vaccines
          - Enter multi-billion PCV market
          - Establish Best-in-Class meningitis portfolio
          - Leverage leading-edge mRNA platform
          - New frontiers
4:30-4:40  Concluding remarks
4:40-5:00  Q&A
Enter multi-billion PCV market

Thomas Grenier
Head of Franchise & Product Strategy

Jean-François Toussaint
Head of Vaccines R&D
Drive growth with PCV21 in attractive pediatric market

Large pneumococcal vaccine market

€6.8bn (Global, 2022)

~80%

~20%

Pediatric

Adult / Elderly

PCV21: growth driver with strong portfolio fit

Focus on pediatric development

First-in-Class PCV20+ in pediatric population

Synergy with Sanofi pediatric vaccine portfolio

Strong collaboration with SK Bioscience

Source: Pfizer, GSK, Merck 2022 Annual Reports; Sanofi estimates
First PCV21 pediatric vaccine extends protection against disease

Serotype composition per vaccine

<table>
<thead>
<tr>
<th>Sanofi PCV21</th>
<th>Pfizer PCV20</th>
<th>Merck PCV15</th>
<th>Pfizer PCV13</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 3 4 5 6A 6B 7F 9V 14 18C 19A 19F 23F 22F 33F 8 10A 11A 12F 15B 9N 2 17F 20</td>
<td></td>
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</tr>
</tbody>
</table>

IPD incremental coverage rate in all ages

<table>
<thead>
<tr>
<th>US 2019+2020</th>
<th>EU 2019+2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVT/Others</td>
<td>37%</td>
</tr>
<tr>
<td>PCV21 non PCV20</td>
<td>27%</td>
</tr>
<tr>
<td>PCV20 non PCV15</td>
<td>6%</td>
</tr>
<tr>
<td>PCV15 non PCV13</td>
<td>14%</td>
</tr>
<tr>
<td>PCV13 non PCV10</td>
<td>26%</td>
</tr>
<tr>
<td>PCV10</td>
<td>29%</td>
</tr>
</tbody>
</table>

Significant residual burden in U.S. pediatrics < 5 years
- ~1,500 cases IPD
- 1.5m Acute Otitis Media cases
- 270k cases of pneumonia

9N serotype provides ~5-7% pts gain in IPD coverage across all ages

NVT: Non-vaccine type  NT: Non-typable  IPD: Invasive pneumococcal disease

61 Vaccines Investor Event
PCV21 (SP0202) Phase 2 designed to enable *pivotal program*

**Study design**

- **4-dose regimen**
  - Months: 2, 4, 6, 7, 12-15, 13-16
  - **Infants 2 Months**
    - PCV21 Formulation #1: n=175
    - PCV21 Formulation #2: n=175
    - PCV21 Formulation #3: n=175
    - PCV13: n=175

**Safety**

**Immunogenicity**

- Post-dose 3 IgG geometric mean concentration and seroresponse
- Post-dose 4 IgG geometric mean concentration

=> Standard evaluation criteria for pivotal trials and registration

**Select formulation for pivotal program**
PCV21 (SP0202) *well-tolerated* in pediatric population

Safety profile comparable with PCV13 across all 4 doses

*Solicited injection site reactions*  
*Solicited systemic reactions*
Favorable PCV21 immune responses when compared to PCV20

Serotypes shared by PCV13, PCV20 and PCV21

IgG GMC ratio and difference % seroresponse vs PCV13

**Post Dose 3: IgG GMC ratio**

- 1
- 3
- 4
- 5
- 6A
- 6B
- 7F
- 9V
- 14
- 18C
- 19A
- 19F
- 23F

**Post Dose 3: Difference seroresponse**

- 1
- 3
- 4
- 5
- 6A
- 6B
- 7F
- 9V
- 14
- 18C
- 19A
- 19F
- 23F

**Post Dose 4: IgG GMC ratio**

- 1
- 3
- 4
- 5
- 6A
- 6B
- 7F
- 9V
- 14
- 18C
- 19A
- 19F
- 23F

PCV21 selected formulation for next phase

**DISCLAIMER:** data from separate studies should be interpreted with care.

- PCV20 Phase 3
- PCV21 Phase 2
- Registration criteria based on PCV13

Vaccines Investor Event
**Favorable PCV21 immune responses** when compared to PCV20

Serotypes shared with PCV20 or unique to PCV21

IgG GMC ratio and difference % seroresponse vs lowest in PCV13 group
Innovative carrier to *break serotype composition ceiling*

Introducing new carrier for 4 serotypes to improve performance

<table>
<thead>
<tr>
<th>1</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6A</th>
<th>6B</th>
<th>7F</th>
<th>9V</th>
<th>14</th>
<th>18C</th>
<th>19A</th>
<th>19F</th>
<th>23F</th>
<th>8</th>
<th>9N</th>
<th>10A</th>
<th>11A</th>
<th>12F</th>
<th>15B</th>
<th>22F</th>
<th>33F</th>
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<tbody>
<tr>
<td><strong>PCV13</strong></td>
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<tr>
<td><strong>PCV21</strong></td>
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</table>

- Carrier protein TT
- Carrier protein CRM\(_{197}\)

Robust performance of the 4 serotypes conjugated to TT

Post Dose 4: IgG GMC ratio

- PCV21 Phase 2
- PCV20 Phase 3

Note: For serotypes 15B and 22F, difference (% and GMC ratio) vs lowest serotype in Prevnar 13

DISCLAIMER: data from separate studies should be interpreted with care.
Phase 2 interchangeability data support **PCV21 as booster**

**Boosting effect is comparable to PCV13 for common serotypes**

**Robust immune response for the additional serotypes**
Ambitious program with *first pediatric PCV20+ vaccine*; clear blockbuster potential

- **Phase 3 starts** in H1 2024
- Expected submission in 2027

- Initiating development of *next generation PCV21+ vaccines*
Establish Best-in-Class meningitis portfolio

Thomas Grenier  
*Head of Franchise & Product Strategy*

Saranya Sridhar  
*Head of Translational Medicine*
Consolidate *MenQuadfi market leadership*

*Best-in-Class MenACWY profile*
- Novel serogroup-specific design, unique chemical and structural features
- Higher serogroup C responses
- Fully-liquid presentation
- Broad age-indication
- Up to 7 years persistence in different age groups

*International roll-out ongoing*
- MenQuadfi registered in **53 countries** and expanding
- WHO pre-qualified

*Leadership in the U.S. with >60% MS*
New clinical evidence reinforces *MenQuadfi’s Best-in-Class* profile

**Immune response vs. competition**

**Adolescents (10-17 years)**
Higher or comparable immune response vs. Pfizer’s ACWY in adolescents

Comparison of hSBA GMT responses 30 days after vaccination\(^1\)

**Infants & Toddlers (2-12 months)**
Higher immune response with 3 doses of MenQuadfi vs. 4 doses of GSK’s ACWY

Comparison of hSBA GMT responses 30 days after vaccination\(^2\)

---

1. Sanofi data on file (MEQ71)
2. Sanofi data on file (MET33)
MenQuadfi *first and only ready-to-use syringe*

- ~80% preference by U.S. HCPs\(^1\) when ready-to-use syringe option is available
- *Unique presentation competitive advantage:* no other ACWY syringe available
- *U.S. FDA submission in July 2023,* available early 2024

Source: Sanofi data on file
MenQuadfi addresses current recommendation for quadrivalent MenACWY immunization in most markets

Complex and various routine recommendations\(^1\) due to different IMD incidence by serogroup, age, geography

<table>
<thead>
<tr>
<th></th>
<th>Infants</th>
<th>Toddlers</th>
<th>Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td></td>
<td></td>
<td>MenACWY (11&amp;16 yrs)</td>
</tr>
<tr>
<td>France</td>
<td>MenB (3 mo)</td>
<td>MenC+B (5 mo)</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>MenB (3,4,6 mo)</td>
<td>MenC+B (12 mo)</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>MenB (3,4,6 mo)</td>
<td>MenACWY (13-15mo)</td>
<td>MenACWY (12/18 yrs)</td>
</tr>
<tr>
<td>Spain</td>
<td>MenC (4 mo)</td>
<td>MenC (12 mo)</td>
<td>MenACWY (12 yrs)</td>
</tr>
<tr>
<td>UK</td>
<td>MenB (2,4 mo)</td>
<td>MenC+B (12 mo)</td>
<td>MenACWY (13/15 yrs)</td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td>MenACWY (12 mo)</td>
<td>MenACWY (14-16 yo)</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>MenACWY (9 mo)</td>
<td>MenACWY (12 mo)</td>
<td>MenACWY (18 yrs)</td>
</tr>
</tbody>
</table>

\(^1\) Published routine vaccination policies. 2. In the U.S., MenB vaccination for 16- to 23-year-old people is a shared clinical decision.

- MenQuadfi currently has the most complete product profile
- Immunization programs expected to evolve over time, including serogroup B adoption
  - Many countries still transitioning from C to ACWY
  - Pace of ACWY switch to pentavalent highly dependent on schedule compatibility, cost effectiveness and impact on public budget
Novel MenB formulation (SP0230) to provide *optimal protection*

**MenB antigen formulation**
- Non-Lipidated fHBP A
- Non-Lipidated fHBP B
- NadA
- Outer Membrane Vesicle
- **4 major antigens** used to cover broad diversity and variable strain expression

**Phase 1/2 clinical study design**

- **Adolescents** 10-17 yo
  - MenB Formulation #1: n=72
  - MenB Formulation #2: n=72
  - MenB Formulation #3: n=72
  - MenB Formulation #4: n=72
  - MenB Formulation #5: n=72
  - MenB Formulation #6: n=72

- **Adults** 18-55 yo
  - Bexsero (MenB GSK): n=72
  - Trumenba (MenB Pfizer): n=72

fHBP A: factor-H binding protein subfamily A; fHBP B: factor-H binding protein subfamily B; NadA: Neisserial adhesin A
MenB *strong phase 1/2 results* demonstrate competitiveness and support move to next phase

### hSBA seroresponse rate¹ – Sanofi MenB vs Bexsero²

<table>
<thead>
<tr>
<th></th>
<th>Vaccine strains²</th>
<th>Cross-protection against strains not in the vaccine³</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MenB Formulation 1</strong></td>
<td>![Chart]</td>
<td>![Chart]</td>
</tr>
<tr>
<td><strong>MenB Formulation 3</strong></td>
<td>![Chart]</td>
<td>![Chart]</td>
</tr>
</tbody>
</table>

- Sanofi formulations were well tolerated
- All antigens are immunogenic
- Breadth of protection reaching expected level

### hSBA seroresponse rate¹ – Sanofi MenB vs Trumenba

<table>
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<tr>
<td><strong>MenB Formulation 3</strong></td>
<td>![Chart]</td>
<td>![Chart]</td>
</tr>
</tbody>
</table>

- Higher point estimates (>+15%)
- Similar (+/- 15%)
- Lower (<15%)

---

1. hSBA seroresponse - % of participants with ≥ 4-fold rise of antibody titer from baseline
2. Tested strains exhibiting one of the Sanofi vaccine antigen
3. Tested strains exhibiting different antigens from the Sanofi vaccine
Strong preclinical data support advancement of MenPenta program in *ready-to-use syringe to phase 1/2 in H2 2023*

- **Liquid MenPenta stability data give high confidence in PFS formulation**
- **No immune interference between MenPenta components (rabbit model)**
- **% of responders demonstrating a 4-fold increase between D0 and D42 in a serum bactericidal assay**

<table>
<thead>
<tr>
<th>B Vaccine strains</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>MenB</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MenPenta</td>
<td>85</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MenQuadfi</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A, C, W, Y vaccine strains</th>
<th>A</th>
<th>C</th>
<th>W</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>MenB</td>
<td>100</td>
<td>100</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>MenPenta</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MenQuadfi</td>
<td>85</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

- **No immune interference between MenB and MenQuadfi antigens**
- **Good stability of the fully-liquid formulation**
- **Advancing MenPenta liquid formulation to phase 1/2 in H2 2023**

Source: Sanofi data on file
Comprehensive and competitive meningococcal portfolio provides new source of growth

- **MenQuadfi Best-in-Class** MenACWY vaccine
- **MenB** formulation demonstrates strong potential for cross-protection across B strains
- Advancing **MenPenta** development in ready-to-use syringe with expected U.S. submission in 2027
Leverage leading-edge mRNA platform

Jean-François Toussaint
Head of Vaccines R&D

Frank DeRosa
Head of Research for mRNA CoE
Built a leading-edge mRNA platform in just 18 months

**Execution**

- 7 mRNA Phase 1/2 clinical trials: *Flu, RSV, platform, 3 LNP* screened
- >600 dedicated employees, of which >250 new recruits
- Extensive external network of academia, industry and government partnerships

**Innovation**

- Innovative antigen, mRNA and LNP designs across viral and bacterial targets
- Highly competitive LNP selected for improved immunogenicity and better tolerability
- Developed high-throughput translational science model with proprietary MIMIC® system to predict clinical outcomes
Accelerated learnings from holistic data integration leveraging AI/ML models

**Antigen design**
- Rationally designed for high immunogenicity and stability

**mRNA design**
- 5 generative and active learning ML models
- Multi features optimization

**LNP Optimization**
- Predictive and generative models developed

**Translational models**
- 1st version of predictive modeling for reactogenic signatures

**Clinical profile**
- Deep understanding

**Adverse events**

**AI/ML models**

**Platform evolution**
- Preclinical prediction

**Immunogenicity & durability**

**Inflammatory profiling**

**Mechanism of action**
Platform now includes **both viral and bacterial protein** targets

Robust preclinical antibodies titers across many target antigens (viral & bacterial)

**Viral**

- RSV
- hMPV
- PIV3

**Bacterial**

- Acne 1
- Acne 2
- Chlamydia

Source: Data on file. rProt = recombinant Protein

Vaccines Investor Event
Leverage *leading-edge mRNA platform* for Best-in-Class / First-in-Class mRNA vaccines and therapeutics

- **Potency**
- **Reactogenicity**
- **Thermostability**
- **Viral Targets**
- **Bacterial Targets**

**Target**
balanced efficacy and tolerability

**Generate**
enhanced HCP and patient experience

**Utilize**
broad spectrum of applications
Our new platform enables improved mRNA performance

**mRNA Sequence Optimization Process**

- 5' cap
- 5' UTR
- Coding Region
- 3' UTR
- Poly (A) Tail

**Increased Translation Efficiency (Polysome Profiling)**

- Control sequence
- Codon optimized

**Increased Protein Expression (Immunofluorescence)**

- Control Sequence
- Codon Optimized

Source: Data on file

Antigen (HA)

- ~ 500,000 sequences generated in-silico
- ~ 1000 Sequences tested in-vitro
- 30+ Sequences tested in-vivo

**mRNA Translation**

<table>
<thead>
<tr>
<th>mRNA Translationally Active Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control sequence</td>
</tr>
<tr>
<td>Codon optimized</td>
</tr>
</tbody>
</table>

**mRNA Sequence Optimization Process**

<table>
<thead>
<tr>
<th>Codon 1</th>
<th>Codon 2</th>
<th>Codon 3</th>
<th>Codon 4</th>
<th>Codon 5</th>
<th>Codon 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUG</td>
<td>GAG</td>
<td>CUU</td>
<td>CGG</td>
<td>AGC</td>
<td>UAG</td>
</tr>
</tbody>
</table>

**mRNA Sequence Optimization Process**

- 5' cap
- 5' UTR
- Coding Region
- 3' UTR
- Poly (A) Tail

Source: Data on file
**All four LNP components** leave significant room for optimization

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ionizable lipid</strong></td>
<td>The <em>ionizable lipid</em> wraps around the mRNA and helps transport and release it to the targeted cell</td>
</tr>
<tr>
<td><strong>Helper lipid</strong></td>
<td>The <em>helper lipid</em> helps create the lipid membrane of the LNP, and it allows for the LNP to easily fuse to the mRNA’s target cell and endosomal membrane</td>
</tr>
<tr>
<td><strong>Cholesterol</strong></td>
<td><em>Cholesterol</em> enhances the stability of the LNP and ensures it is sturdy and rigid. This assists with the introduction of the mRNA into the cells</td>
</tr>
<tr>
<td><strong>PEGylated lipid</strong></td>
<td>Polyethylene glycol, or a <em>PEG lipid</em>, is what helps maintain the overall physical nanostructure of the LNP and protects the mRNA nanoparticles from the body’s natural clearance mechanisms</td>
</tr>
</tbody>
</table>
Sanofi novel science supports *improved LNP and better potency*

**Ionizable Lipid**
- Extensive ionizable libraries developed for improved potency for multiple routes of administration

**Helper Lipid**
- Novel helper lipids demonstrating significant improvements in potency (~2-3x)

**Sterol**
- Novel sterols demonstrating significant improvements in potency (~3-4x)

**PEGylated Lipid**
- Novel PEG alternatives maintaining performance in vivo

**Novel 5th Excipient**
- Significant potency boost with excipient (~4x)

---

**Sanofi novel science supports improved LNP and better potency**

---

**PEGylated Lipid**
- Novel PEG alternatives maintaining performance in vivo

---

**Novel 5th Excipient**
- Significant potency boost with excipient (~4x)
Fast learnings from *diverse clinical trials* with mRNA and LNP

**Clinical trials**

- Unmodified vs modified
- Mono- vs multi-valent
- Multiple targets
- Multiple LNPs (4+)

**Multiple Sanofi LNP candidates**

- LNP1 (Flu)
- LNP2 (Flu)
- LNP3 (Flu)
- LNP2 (RSV)

LNP with unmodified mRNA

LNP with modified mRNA
Sanofi’s proprietary MIMIC® system to increase efficiency of mRNA screening

Preclinical MIMIC Prediction

Clinical Outcomes

log2 fold-change in cytokines

2021  ➔  2023

Unmodified

Modified

Solicited Systemic Reactions (%)

Fever  Headache  Chills  Malaise  Arthralgia  Myalgia

Grade 1  Grade 2  Grade 3

Dose Level 1  Dose Level 2  Dose Level 3  Dose Level 1  Dose Level 2  Dose Level 3  Dose Level 4  Dose Level 5

Modified

Unmodified

Grade 1-2  Grade 3

rHA  Dose Level 1  Dose Level 2  Dose Level 3  IIV4  Dose Level 1  Dose Level 2  Dose Level 3  Dose Level 4  Dose Level 5
**Significant progress** toward improved thermostability

- **Monovalent LNP**
- **Multivalent LNP**
- **Scale-up**
- **Industrial environment**

Prototype LNP demonstrating **12-months+** stability as 2-8°C liquid

QIV LNP demonstrating **~9 months** stability as 2-8°C liquid

**Next step:** Achieve large scale batches
Our **leading-edge mRNA platform** is poised to break grounds in vaccine innovation

Competitive platform in just 18 months with 7 clinical trials...

...innovating across technology... and biology
New frontiers

Dr William Geisler, MD, MPH
Professor of Medicine and Epidemiology,
University of Alabama at Birmingham

Sally Mossman
Head of Vaccine Research Portfolio Strategy
Innovation to address unmet needs in **infectious diseases**

**Chlamydia**
- Dr William Geisler on the burden of chlamydia disease
- Positive data enable selection of final vaccine candidate

**Acne**
- Key preclinical data support clinical evaluation of therapeutic vaccine candidate
- GMP production to enable clinical evaluation ongoing
Dr William Geisler, MD, MPH

Professor of Medicine and Epidemiology,
University of Alabama at Birmingham
Chlamydia Burden and Need for a Vaccine
Chlamydia is the most common bacterial STI worldwide (~129 million new cases annually)

These numbers represent incident cases of chlamydia, gonorrhea, trichomoniasis and syphilis in 2016.

2020: WHO estimated 377 million new cases of four STIs
- Chlamydia: 129 million new cases
- Gonorrhea: 82 million new cases
- Syphilis: 7.1 million new cases
- Trichomoniasis: 156 million new cases
Chlamydia is a chronic infection and most infected persons do not have symptoms or signs of infection.

Women
- <25% Asymptomatic
- >75% Symptomatic

Men
- <50% Asymptomatic
- >50% Symptomatic

Natural Course of Chlamydia in 83 Asymptomatic Colombian Women

~50% of infections persist at 1 year

Molano et al. J Infect Dis. 2005
Chlamydia has important health consequences, and the burden of morbidity is greater in women

Causes upper genital tract inflammation in 10%-15% of women (PID),\(^1,2\) which may be complicated by:

- Infertility (up to 18%)\(^1\)
- Chronic pelvic pain (up to 33%)\(^3\)
- Ectopic pregnancy (3-fold risk)\(^4\)

Associated with adverse pregnancy outcomes\(^4\)

- Miscarriage, stillbirth, premature birth, and low birth weight (1.5-5-fold risk)
- Infection in newborns (eye and lung infection)

Increases risk for HIV acquisition (1.5-2-fold)\(^5-6\)

2. Oakeshott, et al. BMJ. 2010  
Chlamydia control programs provide a comprehensive approach to preventing and treating chlamydia

Chlamydia Prevention Measures
• Abstinence
• Sexual health education
• Barrier methods (e.g., condoms)
• NO VACCINE AVAILABLE

Chlamydia Testing (with highly accurate NAAT)
• Routine screening in young women, MSM, and other women and men at risk
• Diagnostic testing with symptoms/signs

Chlamydia Treatment
• Treatment of patient and partner(s)
• Doxycycline x 7d or azithromycin x 1 effective
• No antibiotic resistance concerns
Control programs have been ineffective in decreasing chlamydia rates, justifying need for a preventative vaccine.

Rates of Reported Chlamydia Cases, U.S., 1984–2021*

(\(^{*}\) Per 100,000)

- Many chlamydia cases go undetected and untreated
- Natural infection does not elicit long-lived protective immunity in most
  - Reinfection occurs in up to 20% within one year\(^{1}\)
- Treatment early in course of infection may impair immunity\(^{2}\)

Thank you

wgeisler@uabmc.edu
Significant direct medical costs in STI attributed to chlamydia

**Chlamydia next to HPV in terms of costs in STIs**

Direct medical costs by infection in U.S.

<table>
<thead>
<tr>
<th>Infection</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>$46 M</td>
</tr>
<tr>
<td>HSV-2</td>
<td>$91 M</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>$144 M</td>
</tr>
<tr>
<td>Syphilis</td>
<td>$174 M</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>$271 M</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>$691 M</td>
</tr>
<tr>
<td>HPV</td>
<td>$775 M</td>
</tr>
<tr>
<td>HIV</td>
<td>$13.7 B</td>
</tr>
</tbody>
</table>

Queensland government in Australia fully recognizes the burden of disease in chlamydia

Supporting our vaccine development through the Translational Science Hub in Queensland

Source: CDC's Sexually Transmitted Disease Surveillance, 2021, sexually Transmitted Disease Surveillance, 2021, accessed May 10
Chlamydia trachomatis (CT) is a bacterium that lives inside human cells. Antibodies and CD4 T cell responses include recognition of multiple chlamydia serovars (serotypes), broad population coverage (HLA: Human Lymphocyte Antigen), and a targeted immune profile with CD4 T cells, IFN-γ producing CD4+ T cells as the primary mediators of protection.

Chlamydia biology requires sophisticated vaccine design.
Innovative multi-antigen vaccine candidate achieves targeted immune profile, moving to phase 1/2 in 2024

**Broad cross-serovar T cell responses**

- Spleen cells secreting Interferon-gamma in mice immunized with mRNA encoding Antigen A, or empty LNP control

**Cross-serovar antibodies recognizing native elementary bodies**

- Elementary body (EB) binding antibodies in sera from mice immunized with mRNA encoding Antigen B, C, D or empty LNP control

Serovar equates to serotype terminology in chlamydia field

103 Vaccines Investor Event
Acne
Acne is chronic inflammatory skin disease and the 8th most common medical condition globally

High burden of disease
- Chronic nature of condition
- Psycho-social impact on patients
- Contribution to antimicrobial resistance
- Economic impact of treatment
- Unmet needs with current treatments

Incidence and prevalence significant and increasing
- 8.6 million prevalent cases in U.S.
- 18.3 million prevalent cases in EU

Chen H. et al. Magnitude and temporal trend of acne vulgaris burden in 204 countries and territories from 1990 to 2019: an analysis from the Global Burden of Disease Study 2019
Layton A. M. et al. Reviewing the global burden of acne: how could we improve care to reduce the burden?
Recent market research points to *gaps in treatment landscape* driving a significant need for novel approaches.

"Isotretinoin has the efficacy, but it’s complicated and has risks – *none of the options we have give us everything we need in one treatment*"

– Dermatologist, Germany

"Acne is *very hard on patients* because it is a disease that everyone can see;...I don’t take it lightly because I know it can have *psychological and social ramifications*"

– Dermatologist, US

Sanofi internal HCP market research, 1Q23
Our ambitious approach in the acne immunotherapeutic space

- Targeted intervention designed to restore a healthy skin microbiome
- Leveraging antigens from Origimm acquisition, enhanced with additional antigen
- Critical functional assays developed and running
- Synergy between Sanofi Vaccines and Pharma Immunology Franchise
- Full speed development of mRNA-based candidate

Recombinant protein antigens obtained through Origimm acquisition validated with strong proof of mechanism data

OPK: opsonophagocytic killing of C. acnes bacteria

<table>
<thead>
<tr>
<th>Antigen</th>
<th>OPK Titer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen 1</td>
<td>$10^6$</td>
</tr>
<tr>
<td>Antigen 2</td>
<td>$10^5$</td>
</tr>
<tr>
<td>Negative control</td>
<td>$10^3$</td>
</tr>
</tbody>
</table>

$10^2$
Therapeutic vaccine addressing **multiple pathogenic mechanisms**

**Acne vulgarum:** skin dysbiosis driven by outgrowth of pathogenic Cutibacterium acnes

- **Corneocyte**
- **Sebum**
- **C. acnes**

**Origimm Antigens**
- Expressed on surface of pathogenic C. acnes strains
- Induce opsonophagocytic killing antibodies to reduce bacterial burden
- Essential adhesin and iron uptake functionality

**Additional Vaccine Antigen**
- Based on key bacterial virulence factor
- Induces antibodies that neutralize the virulence factor, interrupting the inflammatory cascade that drives disease

**Inflammatory cascade**

---


108 Vaccines Investor Event
Positive pre-clinical data support move to phase 1/2 in 2023

mRNA expression of bacterial antigens induces functional immune responses at least equivalent to recombinant proteins

No interference in induced responses with combination of all three mRNAs

OPK: opsonophagocytic killing

Neutralization of inflammatory factor

Antigen 1

Antigen 2

Antigen 3

OPK titers

Sero-neutralization titers

rProt mRNA Negative control rProt mRNA Negative control rProt mRNA Negative control

10^9 10^8 10^7 10^6 10^5 10^4 10^3

1 10 100

mRNA Antigen 1 mRNA Antigen 2 mRNA Antigens 1+2+3 Negative control mRNA Antigen 3 mRNA Antigens 1+2+3 Negative control

10^9 10^8 10^7 10^6 10^5 10^4 10^3

1 10 100

Neutralization of inflammatory factor
Moving at pace to unlock new areas in infectious disease

- Expanding to new disease areas
- Addressing unmet needs
- Leveraging the right technological solutions

*Therapeutic or prophylactic*
*Association of infectious agents with chronic diseases*
*Microbiome*
Conclusion

Thomas Triomphe
*Head of Vaccines GBU*
Sanofi drives *innovation* with BiC/FiC vaccines pipeline

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3</strong></td>
<td>New products approved since Vaccines Investor Event in December 2021</td>
</tr>
<tr>
<td><strong>mRNA</strong></td>
<td>Leading-edge mRNA platform to lift our influenza standard of care and deliver innovation to address unmet needs</td>
</tr>
<tr>
<td><strong>6</strong></td>
<td>New vaccine candidates expected in phase 1/2 trial in 2022/23</td>
</tr>
<tr>
<td><strong>At least 5</strong></td>
<td>First-in-Class / Best-in-Class vaccine candidates expected in phase 3 by 2025 across diverse preventative and therapeutic areas</td>
</tr>
</tbody>
</table>
On a clear path to generate >€10bn sales by 2030

- Launch Beyfortus blockbuster and build BiC RSV franchise
- Continue to win in Influenza
- Enter Pneumococcal market with PCV blockbuster candidate
- Sustain growth of established business
- Introduce our new mRNA vaccines to market

1. At 2023 rate

Sanofi
Vaccines sales
>€10bn
by 2030

113 Vaccines Investor Event
Q&A session Part 2

Thomas Triomphe  
Head of Vaccines GBU

Thomas Grenier  
Head of Vaccines F&PS

Jean-François Toussaint  
Head of Vaccines R&D

Saranya Sridhar  
Head of Translational Medicine

Frank DeRosa  
Head of Research for mRNA CoE

Dr William Geisler, MD, MPH  
Professor of Medicine & Epidemiology  
University of Alabama at Birmingham

Sally Mossman  
Head of Vaccine Research Portfolio Strategy
## Collaborations

<table>
<thead>
<tr>
<th>Name</th>
<th>Developed in collaboration with...</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beyfortus®</strong></td>
<td>AstraZeneca</td>
</tr>
<tr>
<td><strong>Dupixent® itepekimab (IL-33)</strong></td>
<td>Regeneron</td>
</tr>
<tr>
<td>frexalimab</td>
<td>ImmuNext</td>
</tr>
<tr>
<td><strong>VidPrevtyn® Beta</strong></td>
<td>GSK and with funding from Biomedical Advanced Research and Development Authority (BARDA)</td>
</tr>
<tr>
<td><strong>SP0202</strong></td>
<td>SK Bioscience</td>
</tr>
<tr>
<td>Abbreviations</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
</tr>
<tr>
<td>ACIP</td>
<td>Advisory Committee on Immunization Practices</td>
</tr>
<tr>
<td>AE</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>AI</td>
<td>Artificial Intelligence</td>
</tr>
<tr>
<td>BTK</td>
<td>Bruton’s Tyrosine Kinase</td>
</tr>
<tr>
<td>CD</td>
<td>Cluster of Differentiation</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CT</td>
<td>Chlamydia Trachomatis</td>
</tr>
<tr>
<td>dOMV</td>
<td>detoxified Outer Membrane Vesicles</td>
</tr>
<tr>
<td>EB</td>
<td>Elementary Body</td>
</tr>
<tr>
<td>ELISA</td>
<td>Enzyme-Linked Immunosorbent Assay</td>
</tr>
<tr>
<td>ESPID</td>
<td>European Society for Paediatric Infectious Diseases</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>fHBP</td>
<td>factor-H Binding Protein</td>
</tr>
<tr>
<td>GMC</td>
<td>Geometric Mean Concentration</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
</tr>
<tr>
<td>GMT</td>
<td>Geometric Mean Titers</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner or Glycoprotein</td>
</tr>
<tr>
<td>HA</td>
<td>Hemagglutinin</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>HCP</td>
<td>Healthcare Professionals</td>
</tr>
<tr>
<td>HD</td>
<td>High Dose</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HLA</td>
<td>Human Lymphocyte Antigen</td>
</tr>
<tr>
<td>hMPV</td>
<td>Human Metapneumovirus</td>
</tr>
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<td>HPV</td>
<td>Human Papillomavirus</td>
</tr>
<tr>
<td>HSBA</td>
<td>Human Serum Bactericidal Activity</td>
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<tr>
<td>HSV-2</td>
<td>Herpes Simplex Virus type 2</td>
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<tr>
<td>IFN</td>
<td>Interferon</td>
</tr>
<tr>
<td>IgA</td>
<td>Immunoglobulin A</td>
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<td>IgG</td>
<td>Immunoglobulin G</td>
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<tr>
<td>IL-13</td>
<td>Interleukin 13</td>
</tr>
<tr>
<td>IMD</td>
<td>Invasive Meningococcal Disease</td>
</tr>
<tr>
<td>IPD</td>
<td>Invasive Pneumococcal Disease</td>
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<tr>
<td>LNP</td>
<td>Lipid Nanoparticle</td>
</tr>
<tr>
<td>LRTD</td>
<td>Lower Respiratory Tract Disease</td>
</tr>
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<td>LRTI</td>
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</tr>
<tr>
<td>MA-LRTI</td>
<td>Medically Attended LRTI</td>
</tr>
<tr>
<td>ML</td>
<td>Machine Learning</td>
</tr>
<tr>
<td>mNT</td>
<td>micro Neutralization Test</td>
</tr>
<tr>
<td>MoA</td>
<td>Mode of Action</td>
</tr>
<tr>
<td>mRNA</td>
<td>messenger RNA</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>NA</td>
<td>Neuraminidase</td>
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<tr>
<td>NadA</td>
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<tr>
<td>NT</td>
<td>Non-typable</td>
</tr>
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<tr>
<td>OA</td>
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<tr>
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<td>Opsonophagocytic killing</td>
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<td>Pneumonia and Influenza</td>
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<td>Protection Beyond Flu</td>
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<td>PCV</td>
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<td>PFS</td>
<td>Pre-filled Syringe</td>
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<tr>
<td>PIV</td>
<td>Parainfluenza Virus</td>
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<tr>
<td>QIV</td>
<td>Quadrivalent Influenza Vaccine</td>
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<tr>
<td>RP-LC</td>
<td>Reversed Phase Liquid Chromatography</td>
</tr>
<tr>
<td>rProt</td>
<td>recombinant Protein</td>
</tr>
<tr>
<td>RSV</td>
<td>Respiratory Syncytial Virus</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Dose</td>
</tr>
<tr>
<td>SoC</td>
<td>Standard of Care</td>
</tr>
<tr>
<td>STI</td>
<td>Sexually Transmitted Infection</td>
</tr>
<tr>
<td>TEAE</td>
<td>Treatment Emergent Adverse Event</td>
</tr>
<tr>
<td>TNFI</td>
<td>Tumor Necrosis Factor Inhibitor</td>
</tr>
<tr>
<td>TSLP</td>
<td>Thymic Stromal Lymphopoietin</td>
</tr>
<tr>
<td>TT</td>
<td>Tetanus Toxoid</td>
</tr>
<tr>
<td>URTD</td>
<td>Upper Respiratory Tract Disease</td>
</tr>
<tr>
<td>UTR</td>
<td>Untranslated Region</td>
</tr>
<tr>
<td>VFC</td>
<td>Vaccines for Children</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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