

Vaccines Investor Event

Part 2 Leading with innovation

December 1st, 2021



Vaccines Investor Event | Agenda

Introduction		Paul Hudson	Chief Executive Officer			
We Play to Win		Thomas Triomphe	Head of Vaccines GBU			
Growing current	Winning in Influenza	Bill Averbeck	Head of Influenza Franchise			
business	All infant protection against RSV	Kimberly Tutwiler	Head of RSV Franchise			
Q&A session						
Building an innovative & diversified pipeline		Jean-François Toussaint	Head of Vaccines R&D			
Leading with	Unlocking the potential of mRNA	Frank DeRosa	Head of Research for mRNA CoE			
innovation	Broadening the pipeline to	Jean-François Toussaint	Head of Vaccines R&D			
	address unmet needs	Thomas Grenier	Head of Franchises & Product Strategy			
(Conclusion	Thomas Triomphe	Head of Vaccines GBU			
Q&A session						
SANOFI S CoE: Center of Excellence						



Building an innovative & diversified pipeline

Jean-François Toussaint

Head of Vaccines Research & Development





Building an innovative and diversified pipeline to deliver sustainable growth



Opening a new chapter at Sanofi Vaccines, expanding to new disease areas



Leveraging state of the art immunology & antigen design

Selecting the best technology platform for each target

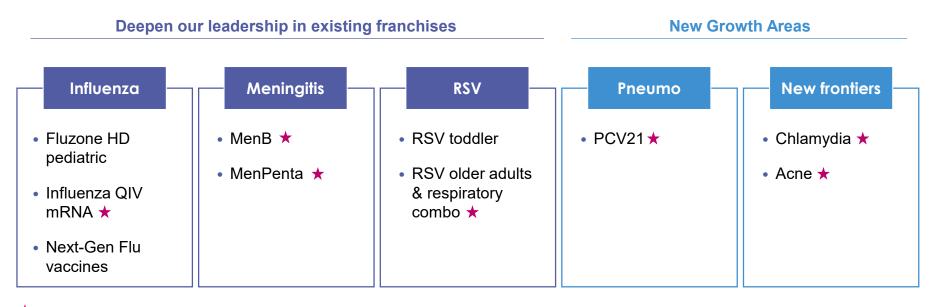
R&D objectives

Rejuvenated pipeline, with **10 new development candidates by 2025** (of which 6 mRNAs)

Focused on first-in-class / best-in-class



Broadening our pipeline & opening new areas for growth



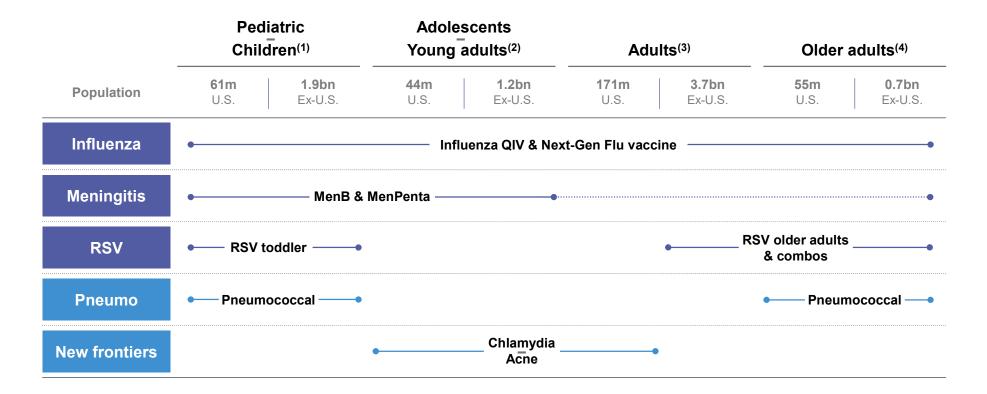
★ = New

Expanding research on additional vaccines candidates against chronic diseases

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RSV: Respiratory syncytial virus PCV: Pneumococcal conjugate vaccine HD: High-Dose QIV: Quadrivalent influenza vaccine

Innovation addressing a large part of the population



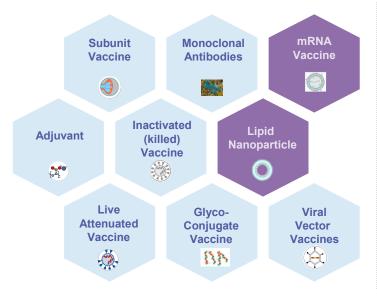
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(1) 0 – 14 years old (2) 15 – 24 years old (3) 25 – 65 years old (4) 65+ years old Source: Population estimates, The World Bank

We added mRNA to our state of the art toolbox

Established platforms

- Broad range of antigen targets
 - Viral & bacterial
 - Protein & polysaccharide
- Proven efficacy across multiple diseases & populations
- **Proven tolerability** from babies to older adults



mRNA & LNP platforms

- Restricted to protein-based antigens
- Particularly well suited for (respiratory) viral pathogens
- Fast to clinic & low CMC costs
- Potential to facilitate multicomponent vaccines

We select the best platform for each target





Unlocking the potential of mRNA

Frank DeRosa

Head of Research mRNA CoE





CoE: Center of Excellence

Sanofi mRNA Center of Excellence A biotech environment with Sanofi's powerhouse

🎝 SANOFI

- Deep vaccine & antigen design expertise
- Well-established development platforms
- Expertise in running clinical trials
- Global manufacturing scale

Translate BIO

- Strong mRNA & LNP know-how
- Proprietary algorithms & large LNP database
- Large scale material production capabilities

mRNA Center of Excellence

Moving fast beyond 1st generation mRNA

- **400 dedicated employees** in the U.S. (Cambridge) and France (Lyon)
- **Positive clinical results** from COVID-19 and influenza monovalent mRNA candidates
- **Pivot to modified mRNA achieved;** clinical trials planned to start in 2022
- Expansion of proprietary database ongoing internally & with partnerships

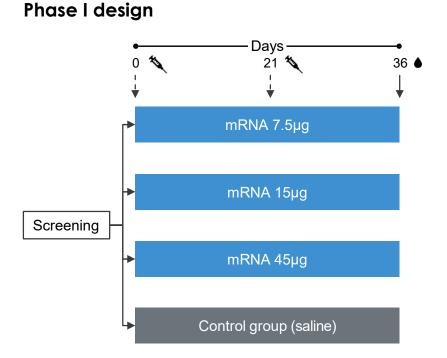


First clinical trial with our proprietary mRNA & LNP platform

Unmodified mRNA & proprietary LNP, using COVID-19 as a reference antigen

Optimized unmodified mRNA encoding prefusion full-length SARS-CoV-2 spike protein

Proprietary LNP with customized composition and ratio

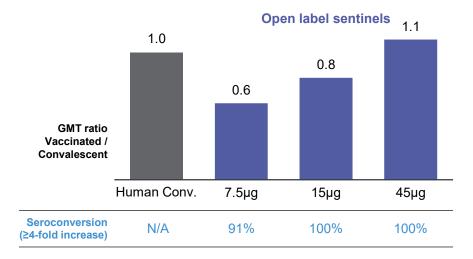




Platform potential confirmed by positive interim results

100% seroconversion for all doses \geq 15µg

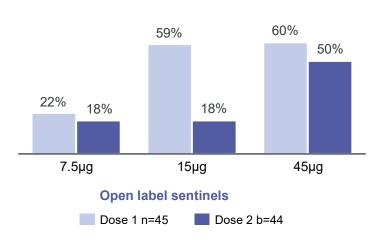
Pseudovirus nAb to D614G 14 days post-dose 2 (SARS-CoV-2 seronegative participants, n=41)





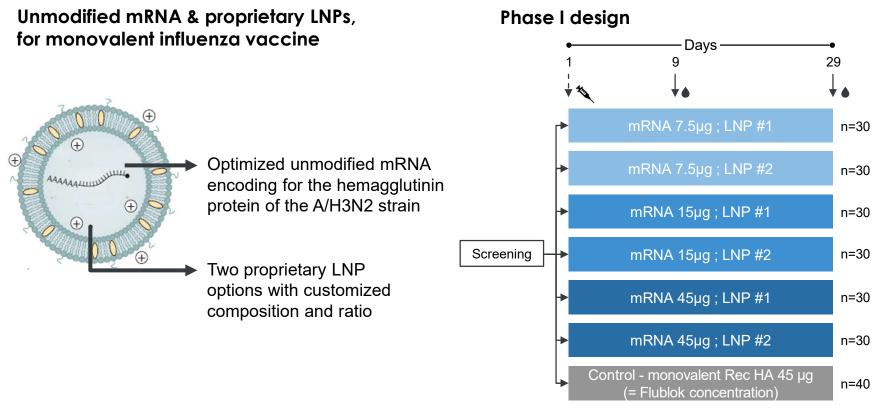
GMT: Geometric mean titer Source: Data on file

Tolerability profile in line with other unmodified mRNA COVID-19 vaccines



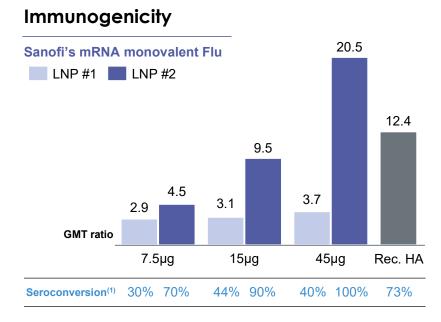
Grade 3 adverse events

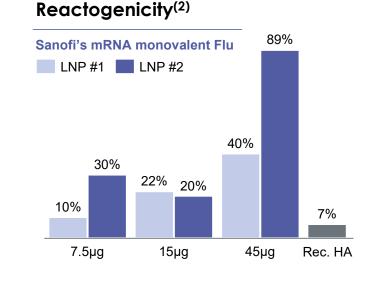
Progressing to clinic with influenza



SANOFI 🧳 LNP: Lipid na

First evidence that mRNA could work for influenza, pending improved reactogenicity





LNP # 2 identified as a promising candidate for influenza vaccine



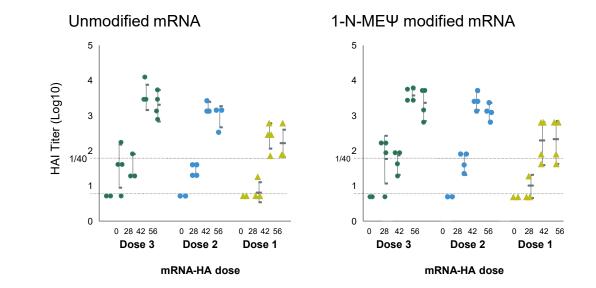
Rec. HA: Recombinant HA HA: Hemagglutinin GMT: Geometric mean titer (1) Seroconversion: proportion of participants with D01 < 10 (1/dil) and post-titer >=40 (1/dil) or D01 >=10 (1/dil) and post-titer >= 4-fold increase (2) Grade 3 solicited reactions Source: Data on file

Successfully pivoted to modified mRNA

Switch to modified mRNA achieved

Similar immunogenicity with modified mRNA in NHP

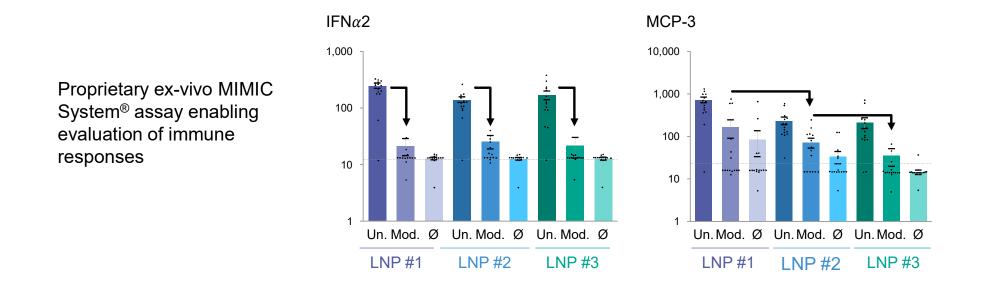
- Pre-clinical data generated in multiple animal models
- · GMP material produced
- On track to start clinical trials in influenza
 - H1 2022 for monovalent
 - H2 2022 for quadrivalent



First clinical data with modified mRNA expected in 2022

SANOFI Source: NHP: Non-human primate Note: Study conducted in NHP with escalating two doses schedule (Day 0 and Day 28) - mRNA encoding for Flu Hemagglutinin Source: Data on file

Biomarkers show clear path to reduce reactogenicity with modified mRNA and optimized LNPs

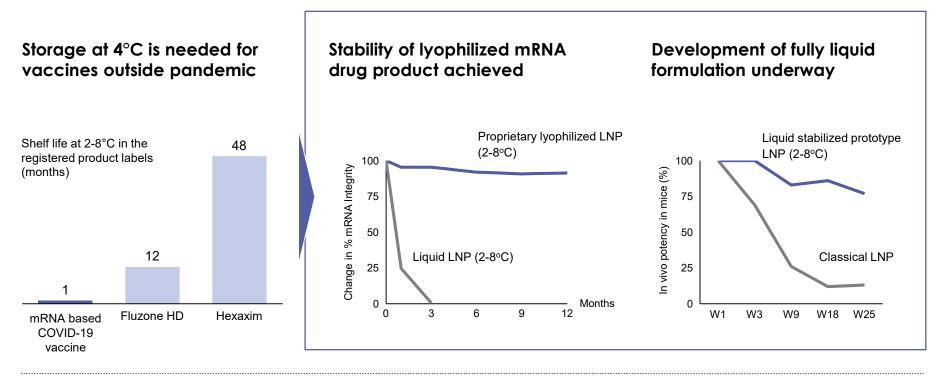


Modified mRNA & LNP optimization expected to reduce reactogenicity in the clinic



LNP: Lipid nanoparticles \emptyset : no mRNA MIMIC: Modular Immune in vitro Construct Note: IFN α 2 and MCP-3 presumed biomarkers of reactogenicity Source: Data on file

Overcoming mRNA thermostability challenges

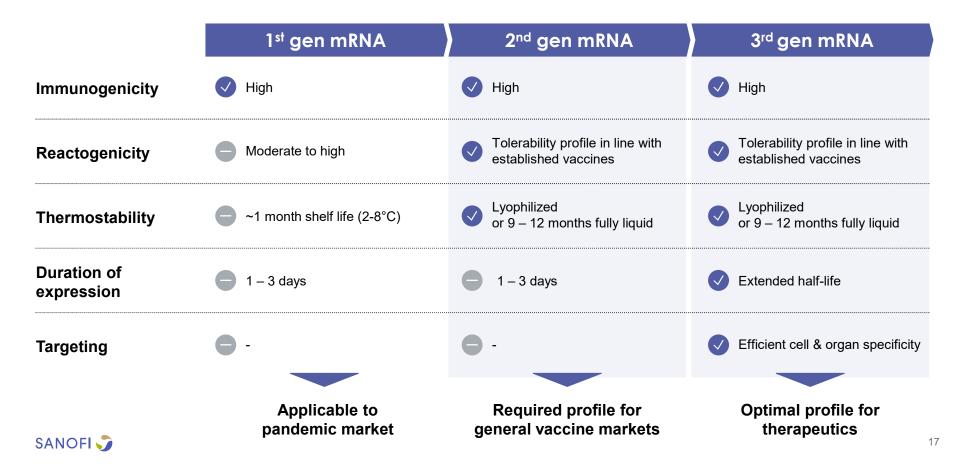


Ready to go with lyophilized



Note: Fluzone HD: Egg-based influenza vaccine Hexaxim: 6-in-1 combination pediatric vaccine Source: Data on file

Breaking barriers to unlock mRNA potential





Jean-François Toussaint Head of Vaccines Research & Development

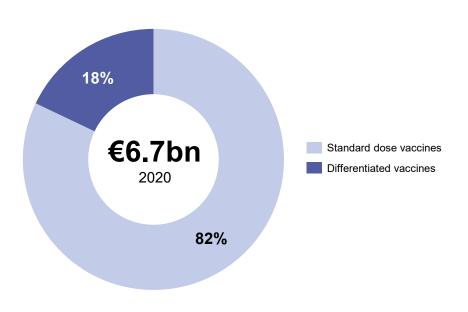
Broadening the pipeline to address unmet needs



Thomas Grenier Head of Franchises & Product Strategy



Influenza: further raising the bar



Market overview

Sanofi strategy to keep winning in flu

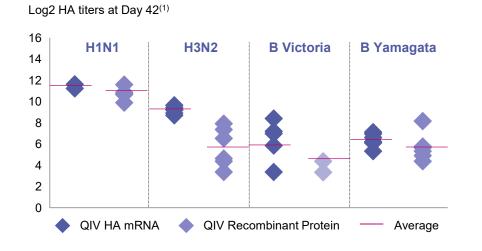
- Accelerated mRNA QIV Influenza development
- Raising the bar further with Next-Gen Flu
 - Machine Learning for better strain selection
 - Expanding on neuraminidase to induce greater protection



QIV: Quadrivalent influenza vaccine Source: Sanofi published sales and market estimates at 2020 exchange rate

First milestone achieved for Sanofi mRNA QIV

Pre-clinical data generated with unmodified mRNA



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Pivoted to modified for final candidate

- Optimized modified mRNA sequence
- Encoding for 4 HA proteins
- Optimized LNP to reduce reactogenicity



LNP: Lipid nanoparticles HA: Hemagglutinin (1) Immunogenicity response in ferrets Source: Data on file

Influenza mRNA QIV development with objective to demonstrate Protection Beyond Flu

Phase I/II – Targeted initiation in 2022

- Two age cohorts (18-64yo & 65yo+)
- Dose-selection trial
- Comparison against standard of care

Selection of final composition for each population

Phase III – Targeted Initiation in 2023

- Quadrivalent vaccine based on WHO selected strains
- · Comparison to standard of care

Registration trial designed to demonstrate vaccine efficacy & build safety database

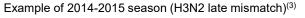


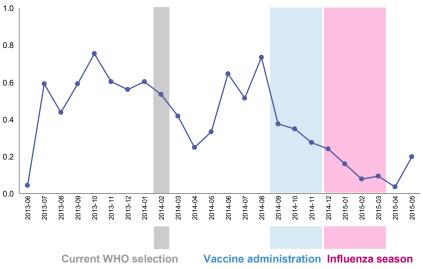
Later strain selection not the solution for improved efficacy

Season Predominant strain Vaccine strain to predominant in adults $\geq 65yo^{(1)}$ circulating strain similarity^(1, 2) A/H3N2 (80.4%) 2010-11 97% 2011-12 A/H3N2 (87.0%) 82% 2012-13 A/H3N2 (86.4%) 100% 2013-14 A/H1N1 (57.2%) 100% 2014-15 A/H3N2 (90.6%) 19% 2015-16 A/H1N1 (48.4%) 100% 2016-17 A/H3N2 (79.0%) 97% 2017-18 A/H3N2 (69.4%) 93% 2018-19 A/H3N2 (53.3%) 11% 2019-20 A/H1N1 (71.0%) 54%

Only 2 out of past 10 years with strain mismatch

Shift in strain dynamic can occur late in season







(1) Adapted from Lee J, Lam J, Shin T, et al. Vaccine 2021 for season 2010-11 to 2018-19 data and from CDC FluView Summary ending July 25, 2020 for season 2019-20 data; Determined using national CDC viral surveillance data on adults 65 years of age and older (2) Antigenic Similarity of Reference Vaccine Strain to Predominant Circulating Strain based on CDC data on viral antigenic characterization comparing reference vaccine strains to circulating viruses; mismatched seasons includes seasons of antigenic mismatch (2009–10, 2014–15, 2018–19) as well as seasons where egg-adapted vaccine strains may have affected vaccine effectiveness (2012–13, 2016–17, 2017–18) (3) GISAID data analysis

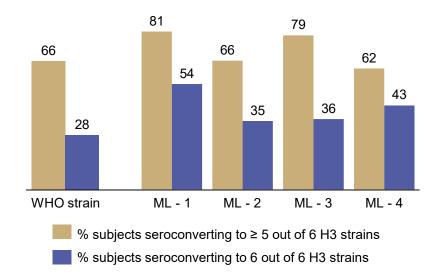
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Striving for better strain selection with Machine Learning

Generation > Soc(2) Soc(2) Soc(2) Soc(2) Sequence PC1

Antigens selected for cross-clade protection

Higher seroconversion for ML-selected antigens⁽¹⁾



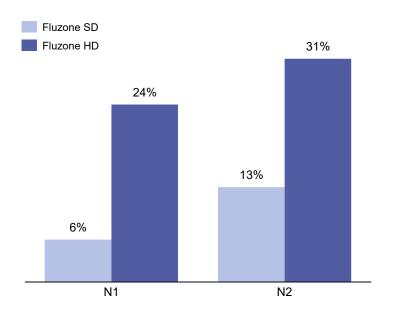
ML selected antigens showed greater breadth in Phase I translational study



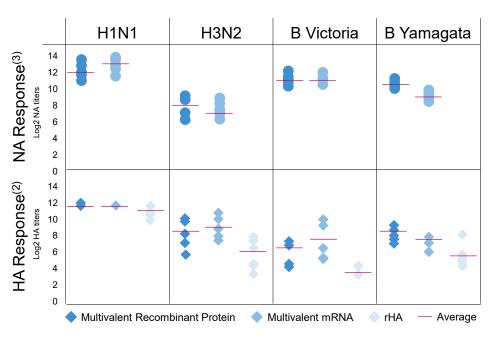
PC: Principal component SoC: Standard of care ML: Machine learning (1) Immunogenicity was assessed via a panel of 6 antigenically distinct influenza viruses from both 3C.2 and 3C.3 clades, isolated in 2016 and 2017; n=30 participants per arm (healthy adults aged 18-30) (2) Statistical significance ratio of 1.35x

Exploring the potential of neuraminidase to further build **Protection Beyond Flu**

Fluzone SD/Fluzone HD already increase anti-NA titers⁽¹⁾



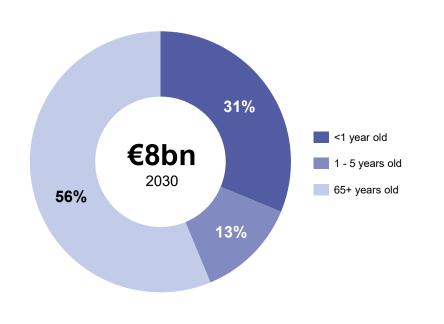
Exploring combined HA + NA multivalent vaccines Response in ferrets of multivalent protein and mRNA vaccines





NA: Neuraminidase HA: Hemagglutinin rHA: recombinant Hemagglutinin (1) Defined as ≥2-fold increase in enzyme-linked lectin assay; Graph shows proportion of subjects developing increase in anti-NA titers (2) Microneutralization assay (3) NA inhibition assay Source: Cate, Thomas R et al. Vaccine (2010); data on file

Respiratory Syncytial Virus: protection across all age groups



Best-in-class protection for all ages



Nirsevimab: best-in-class mAb for *All Infant Protection* in first season



RSV toddler: first-in-class Live Attenuated Virus vaccine for second season onwards



RSV older adults: initiating standalone mRNA vaccine, and paving the way for respiratory combos in older adults

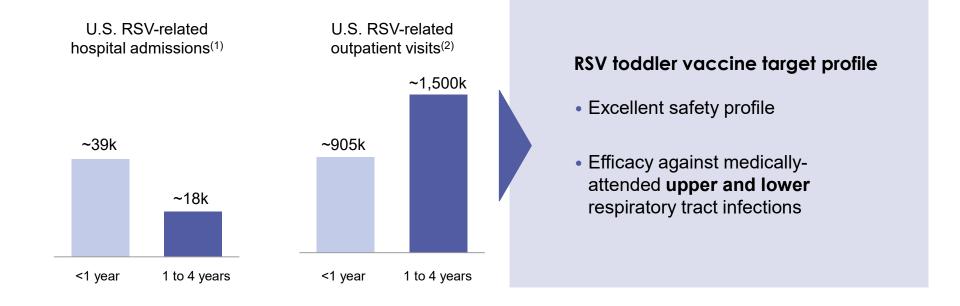


Market overview

mAb: monoclonal antibody Source: Sanofi forecast

RSV burden does not stop after the first season







Note: Internal analysis based on following studies and World Bank 2020 demographic data (1) Rha B, Curns AT, Lively JY, et al. Respiratory Syncytial Virus-Associated Hospitalizations Among Young Children: 2015-2016. Pediatrics. 2020 (2) Emergency and Pediatric practices RSV-related outpatients estimate - Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med. 2009

FiC RSV toddler vaccine designed by reverse genetics





Ongoing Phase I/II in U.S. and Latin America (n=360 participants) – read-out expected in 2022



FiC: First-in-class Source: Data on file

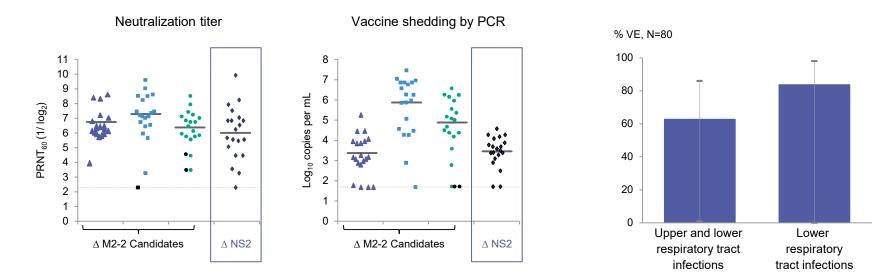
Clinical data shows evidence of efficacy by reducing medically attended acute respiratory illnesses



ΔNS2 vaccine candidate selected for further development

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Evidence of efficacy⁽¹⁾ for both upper and lower respiratory tract infections



VE: vaccine efficacy PRNT: plaque reduction neutralizing titer PCR: polymerase chain reaction

(1) Efficacy measured and displayed across all candidates and not just $\Delta NS2$; p<0.05 significance for VE was observed for Upper and lower respiratory tract infections, however the Placebo group was small with 62 subjects of which 11 experienced RSV-related medically attended acute respiratory Illness (18%) Source: Ruth Karron et al; Am J Respir Crit Care Med 2021

RSV in older adults: addressing a large burden



	Estimated U.S. outpatient acute infection amid 65yo+	Estimated U.S. hospitalizations amid 65yo+	Virus evolution	
RSV	1,041k ⁽¹⁾	105k ⁽²⁾	Low	 Init add Lov pro
HMPV	603k ⁽¹⁾	88k ⁽²⁾	Low	Oppo • Cui
PIV	329k ⁽¹⁾	82k ⁽²⁾	Low	to I • Pot effe
Influenza	1,808k ⁽¹⁾	204k ⁽³⁾	High	

- Initiating standalone RSV mRNA vaccine to address high burden of disease in older adults
- Low variability of RSV may allow for multiyear protection

Opportunity for RSV-based combos

- Cumulated burden of RSV and HMPV comparable to Influenza
- Potential for additional convenience and costeffectiveness benefits

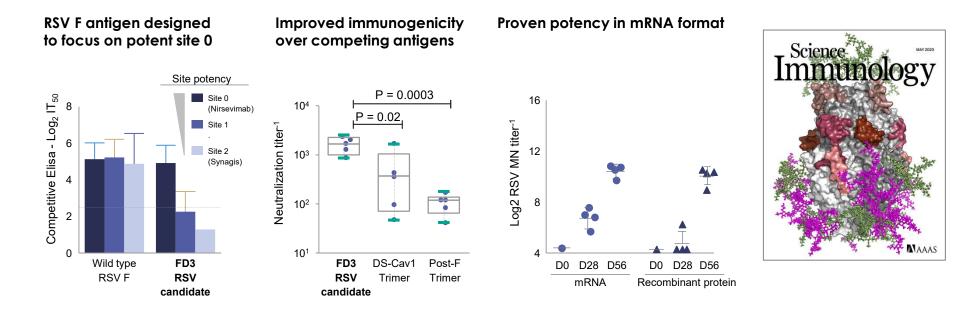
HMPV: Human metapneumovirus PIV: Parainfluenza viruses



(1) Estimate based on World Bank 2020 demographic data and on following study: Jackson ML, Starita L, Kiniry E, et al.. Clin Infect Dis. 2021 (2) Estimate based on World Bank 2020 demographic data and on following study: Sieling, William D et al. "Comparative incidence and burden of respiratory viruses associated with hospitalization in adults in New York City." Influenza and other respiratory viruses vol. 15,5, 2021 (3) CDC data, 2018-2019 flu season

Best-in-class RSV antigen through innovative design





Initiating Phase I with modified mRNA in 2022



State of the art HMPV antigen candidate identified



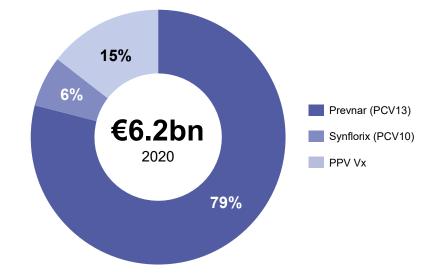
Cutting edge antigen design Proven potency in mRNA format Sanofi proprietary mAb focused on most potent site (Site 0) Log₂ HMPV MN titer⁻¹ Log₂ HMPV MN titer⁻¹ 16 16 4.5-fold 2.9-fold 12 12 8 8 **HMPV F** 4 Gen1⁽¹⁾ preF Gen2 preF Gen3 preF D28 D56 D28 D56 D0 D0 Viral membrane protein protein protein Gen3 preF Gen1 preF mRNA protein

Initiation of Phase I with RSV older adults combo planned for 2023



mAb: monoclonal antibody HMPV: Human metapneumovirus Note: Figure is from manuscript in preparation through SP/UT collaboration. SP innovation (1) Gen1 was unstable, necessitating next generation designs Source: Data on file

Pneumococcal: more serotypes for better protection



Large established market

Strong fit with existing franchises

- Synergy with pediatric and older adult portfolio
- State of the art formulation expertise with multi-valent vaccines
- Partnership with SK Bioscience
 - Complementary capabilities
 - Investment and risk sharing

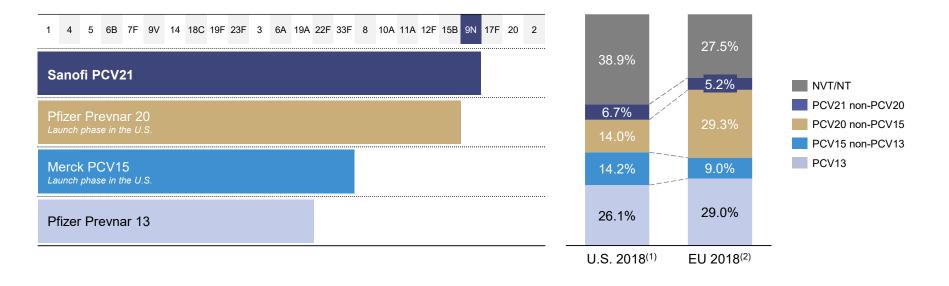


Source: Pfizer, GSK, Merck 2020 Annual Reports

Raising the bar with PCV21 candidate

Serotype composition per vaccine

IPD coverage in all ages by serotype (%)



Addition of 9N serotype allowing for ~5-7% pts gain in IPD coverage



NVT: Non-vaccine type NT: Non-typable IPD: Invasive pneumococcal disease (1) All age groups - ABC data 2018. Metcalf et al. Clin Infect Dis. 2021 Jun 15;72(12):e948-e956 (2) All age groups - https://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=40

Extensive Phase II program across all age groups



Infant Primary

n=700

- 2-4-6 months primary series & booster dose
- 3 PCV21 formulations vs. PCV13

n=140
Booster dose for toddlers having received 3 doses of PCV13

Toddler

• 3 PCV21 formulations vs. PCV13



Adult \geq 50 years old

n=750

- Subjects naïve to prior PCV vaccination
- 3 PCV21 formulations vs. PCV13 & Pneumovax23

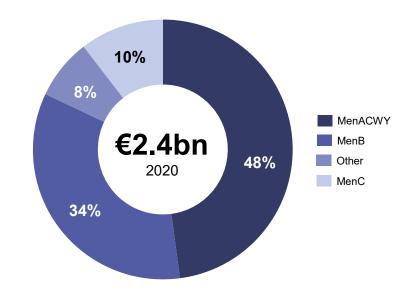
Read-out in all 3 populations expected end of 2022; Phase III initiation planned in 2023



NCT04398706: Study of a Pneumococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Toddlers and Infants. (Sanofi, phase 2 trial, PSK00008, n = 840, recruiting, estimated study completion date July 2023) NCT04583618: Study of a Pneumococcal Conjugate Vaccine in Adults Aged 50 to 84 Years (Sanofi phase 2 trial PSK00009, n = 750; Estimated study completion data Jan 2022)

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Meningitis: Strengthening our leadership



Market overview

- Established leader with Menactra in the U.S.
- MenQuadfi as a new standard in MenACWY, with superior serotype C response to ease market conversion to quadrivalent
- Aiming for competitive MenB with broader strain coverage & longer duration of protection
- Paving the way for best-in-class MenPenta in fully liquid format



MenQuadfi as a new standard in MenACWY

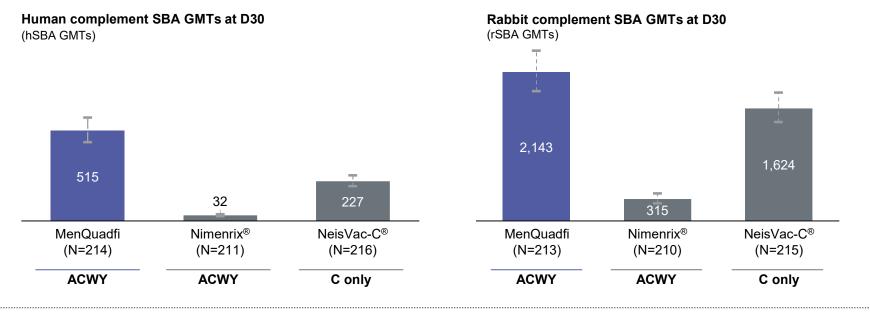
			MenQuad Sanofi (ACW)		Menveo GSK (ACWY)	Nimenrix Pfizer (ACWY)
0	Enhanced immune with superiority aga in toddlers	inst MenC			\mathbf{X}	\mathbf{X}
٥٥	Fully liquid quadri				(1)	$\mathbf{\times}$
(႐ိ)	Broadest age indication	U.S. EU Int'l	≥2 yo ≥12 months old ≥12 months old	≥6 weeks as of 2025	2 months to 55 yo ≥2 yo ⁽²⁾ ≥2 yo	Not registered ≥6 weeks ≥6 weeks



(1) Submission for a liquid form announced in Q3 2021
(2) Indications as of 2 months old in some countries (using US file)

MenQuadfi is the first & only ACWY vaccine to demonstrate superior immune response against serogroup C

Enabling switch from MenC to MenACWY without compromising on serotype C



Paving the way for MenPenta

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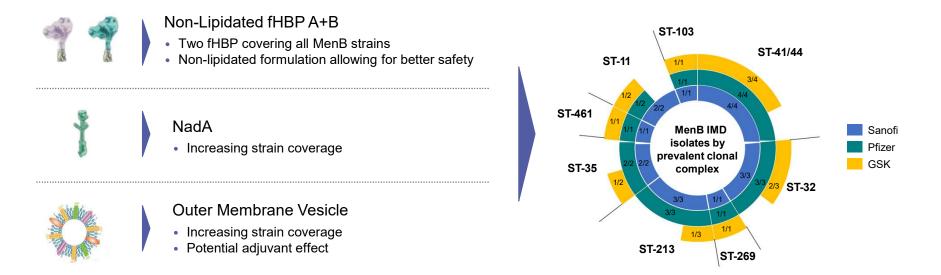


SBA: Serum bactericidal assay - Per-protocol analysis set GMT: Geometric mean titer Source: Knuf et al, (2021): Meningococcal serogroup C (MenC) immune response of a novel tetanus toxoid conjugate quadrivalent meningococcal vaccine (MenACYW-TT) compared to a quadrivalent (MCV4-TT) or monovalent (MenC-TT) meningococcal vaccine in healthy meningococcal vaccine-naïve toddlers

Novel MenB vaccine aiming for increased protection

MenB antigen formulation

Broader coverage of MenB strains⁽¹⁾



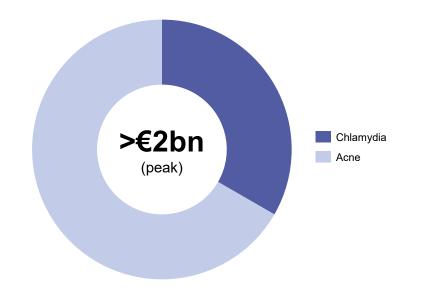
MenB Phase II read-out expected in 2022 – MenPenta Phase I initiation in 2023



IMD: Invasive meningococcal disease fHBP: Factor H binding protein NadA: Neisserial adhesin A (1) Pre-clinical assessment of Serum Bactericidal Antibodies (SBA) against MenB IMD isolates; 18 strains identified as relevant with 1 secondary strain not tested in the preclinical study (not suitable with Research hSBA assay) Source: Pre-clinical study in animal model: Assessment of Serum Bactericidal Antibodies against an epidemiology relevant panel of MenB invasive clinical isolates build by key Reference Laboratories & Representative of current MenB molecular epidemiology

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Pioneering science to open new growth areas



Market overview (estimate)

Delivering first-in-class vaccines

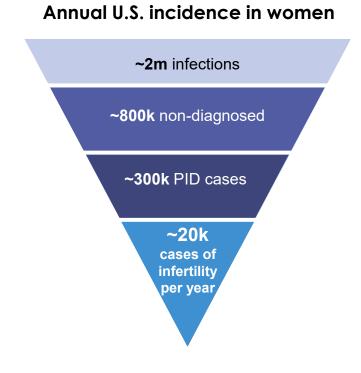
• Chlamydia: tackling the most common infectious cause of female infertility

• Acne: first immunotherapy to treat acne



Source: Sanofi forecasts

Chlamydia: a silent cause of infertility in women



Overwhelming burden in young women

- 69% of estimated annual cases amid young women aged 24 years old or less
- Undiagnosed cases can lead to severe complications, particularly in women
 - Pelvic Inflammatory Cases
 - Tubal infertility
 - Ectopic pregnancy
 - Chronic pelvic pain

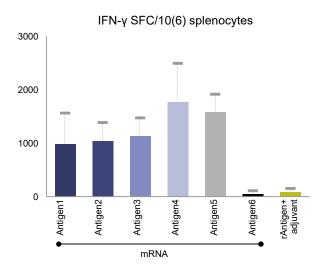
PID: Pelvic inflammatory disease



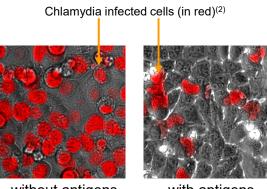
Source: Multiple sources for estimate reconstitution: CDC - Sexually Transmitted Disease Surveillance, 2019 & Chlamydia Fact Sheet, 2018; Land JA, Van Bergen JE, Morré SA, Postma MJ, Hum Reprod. Update, 2010; Price MJ, Ades AE, De Angelis D, et al. Am J Epidemiol., 2013 ; Heisterberg L. Obstet Gynecol., 1993; Ades AE, Price MJ, Kounali D, et al. Am J Epidemiol., 2017; World Bank demographic data 2020

Chlamydia: mRNA best-suited platform to deliver desired immune response

Optimized antigen for strong CD4 T-cells response⁽¹⁾



Selecting additional antigens to prevent Chlamydia entry in endocervical cells



without antigens

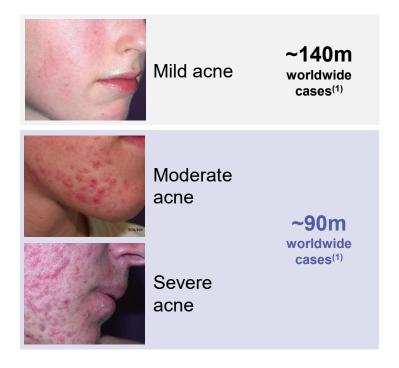
with antigens

mRNA-based multi-component vaccine Phase I launch expected in 2023

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(1) Superior IFN-γ producing T cell with mRNA vs adjuvanted rAntigen (2) High throughput screening of neutralizing IgG and real time monitoring of infection kinetics in endocervical cell line with genetically engineered Chlamydia t. strains Source: Data on file

Acne: a stigmatizing condition



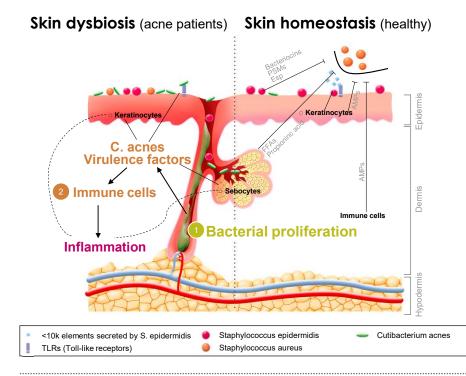
- Significant psychological impact
- Current SoC (oral isotretinoin) with severe side effects
- Significant out-of-pocket expenses (\$360-\$720⁽²⁾ / year in the U.S.)
- P. acnes bacterium also associated with **several** conditions beyond acne:
 - Other dermatological conditions⁽³⁾
 - Medical device-related infections⁽⁴⁾
 - Prostatic inflammation thought to contribute to prostate cancer⁽⁵⁾



(1) Source: IHME. GBD Results Tool; http://ghdx.healthdata.org/gbd-results-tool (2) Sanofi internal analysis (3) Bojar and Holland, 2004; Kurokawa et al., 2009; Barnard et al., 2016 (4) Piper KE et al, J Clin Microbiol. 2009;47(6):1878-1884; Niazi SA et al, Clin Oral Investig. 2016;20(8):2149-2160 (5) Cohen RJ et al, J Urol. 2005;173(6):1969-1974

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Immune system plays a significant role in moderate-tosevere acne



Origimm's antigen induce a functional immune response against C. acnes virulent strains

C. acnes phylotype	Origimm's antigens
IA1	+++
IA2	+++
IB	++
IC	+++
II	++
	(+)

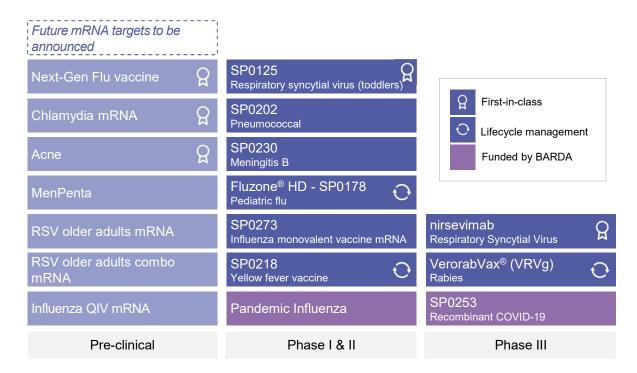
Opsonophagocytic killing by antigen specific mouse sera

Vaccine solution as a first immunotherapy to safely treat moderate-to-severe acne

SANOFI Source: Adapted from Fournière M et al., Microorganisms 2020

Building an industry leading pipeline in Vaccines

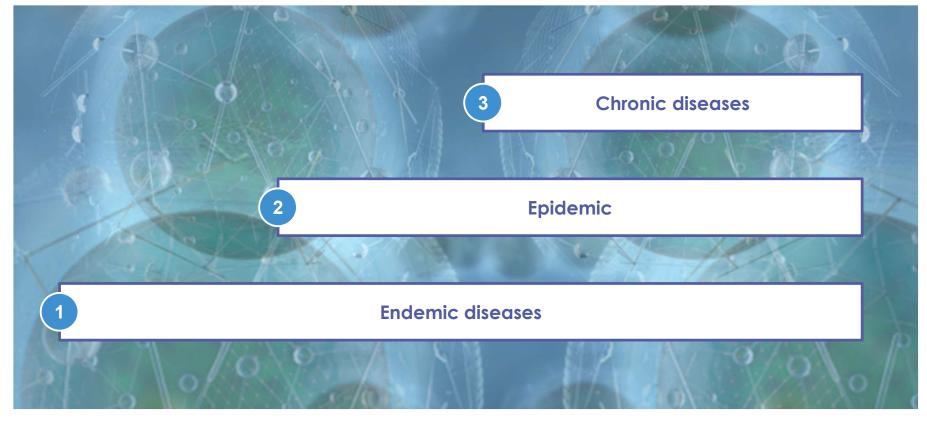
- Target to advance 10 clinical candidates by 2025, incl. 6 mRNA vaccines
- Opportunity to be first-in-class and lead in several new therapeutic fields
- Right mix between LCM, proven targets and breakthrough vaccines





LCM: Lifecycle management SP0148 HSV Type 2 vaccine not indicated above; as it will be discontinued after Phase I completion SP0273 monovalent mRNA Influenza vaccine will be discontinued after Phase I completion

Opening a new chapter for Sanofi Vaccines R&D



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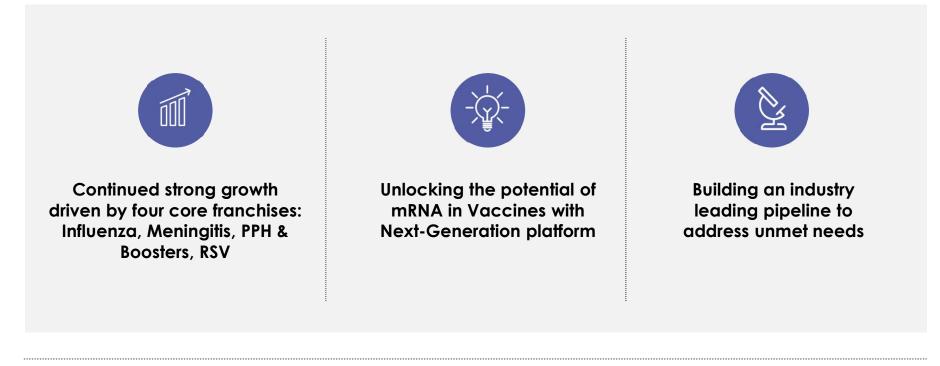


Conclusion

Thomas Triomphe Head of Vaccines GBU



Our ambition in Vaccines



More than doubling Vaccine sales by 2030⁽¹⁾



(1) Vs. 2018, risk adjusted, internal estimate

Q&A session | Leading with innovation



Thomas Triomphe Head of Vaccines GBU



Jean-François Toussaint Head of Vaccines R&D



Frank DeRosa Head of Research for mRNA CoE



Thomas Grenier Head of Franchises & Product Strategy



Jon Heinrichs Head of R&D RSV Franchise