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Introduction to Sanofi Vaccines R&D

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Scientific Affairs*



UIDP

Nov 7, 2024

*DC is an employee and shareholder of Sanofi

Agenda

01 Who we are
SANOFI VACCINES

02 R&D Strategy
FORTIFY, EXPAND, PIONEER

03 Innovations at Sanofi Vaccines
MRNA, NOVEL VACCINE CANDIDATES

04 How to Partner
OPEN INNOVATION, BD DEALS

05 Conclusion
CONTACTS



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Sanofi's *four global business units*



Scientist
Nizar El-Murr



SPECIALTY CARE

- Immunology
- Rare Diseases/
Rare Blood Disorders
- Neurology/
Multiple Sclerosis
- Oncology



GENERAL MEDICINES

- Autoimmune Type 1
Diabetes
- Type 2 Diabetes
- Cardiovascular
- Established Products
- Transplant



VACCINES

- Influenza
- Polio Pertussis
and Hib
- Boosters
- Meningitis
- Travel & Endemic
- RSV



CONSUMER HEALTHCARE

- Allergy
- Cough, Cold & Flu
- Pain Care
- Digestive Wellness
- Physical & Mental
Wellness

Sanofi's Vaccines *in numbers*



500 million
people vaccinated annually
with our vaccines, worldwide



13
vaccine manufacturing sites
in 8 countries



2.5 million
vaccine doses supplied,
every day



7.5 billion €
in sales in 2023



Our vaccines
are available in about
150 countries



1 billion €
invested in vaccines
R&D each year



395 million
polio vaccine doses supplied
to UNICEF since 2014

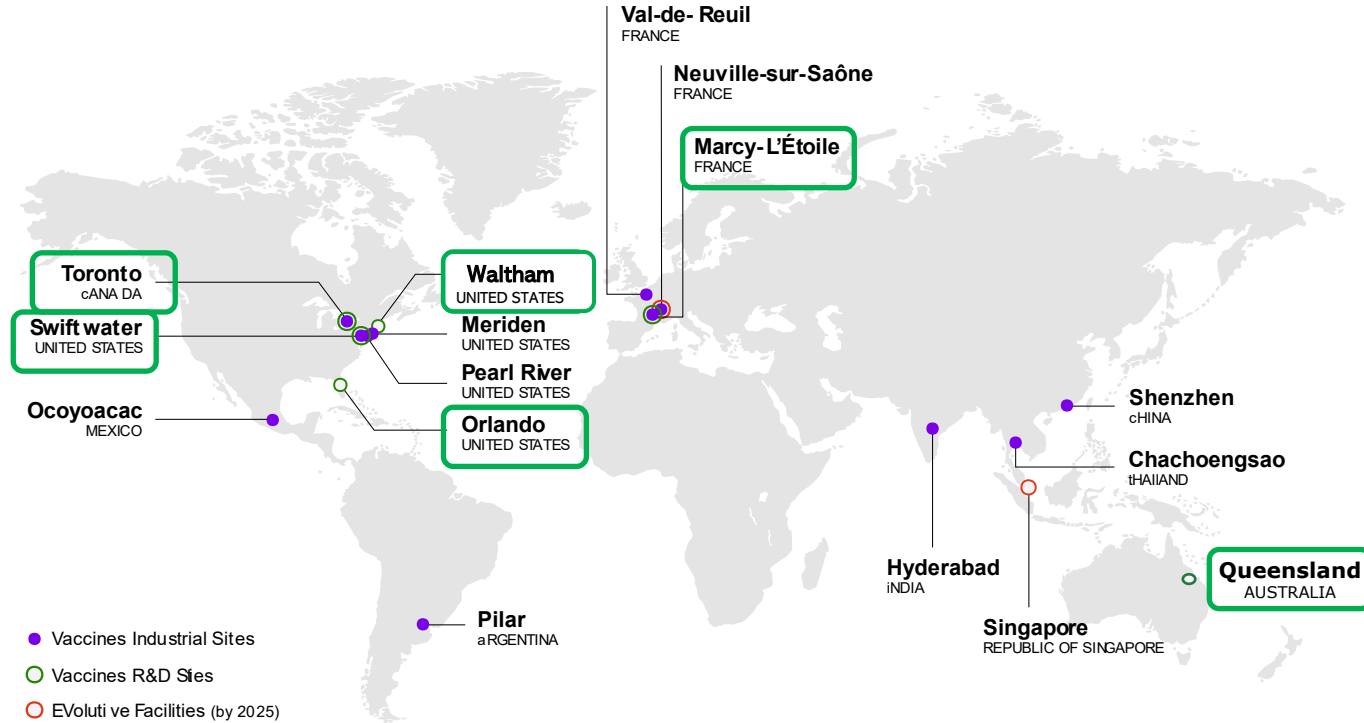


A world leader
in **influenza** and
pediatric vaccines

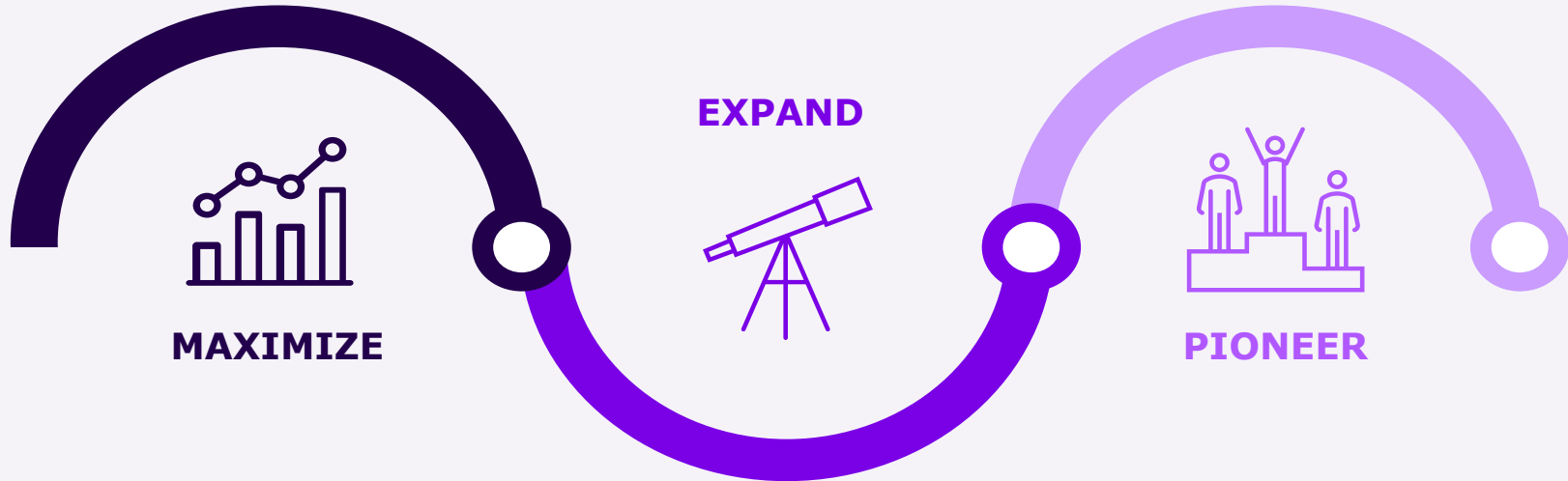


Our Vaccines *footprint*

6 Global R&D Sites



Our Vaccines *pipeline strategy*



MAXIMIZE

Fortify & extend our competitive advantage

- Flu
- Pediatric combos
- Meningococcal
- Travel and Endemic

EXPAND

Win in new* markets with competitive products

- Pneumococcal
- RSV
- COVID-19
- Respiratory combos

PIONEER

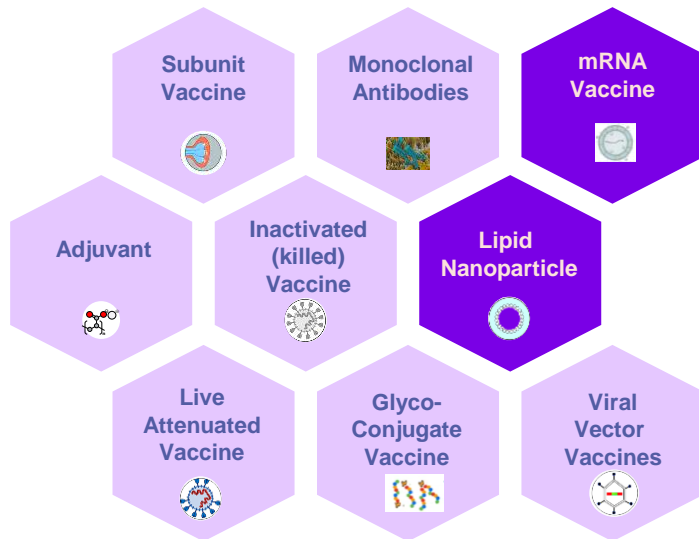
Pioneer research in novel diseases with unmet needs

- ExPEC - E. Coli sepsis
- Acne
- Chlamydia

We select the best vaccine platform for each target

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

- Restricted to **protein-based antigens**
- Particularly well suited for (respiratory) **viral pathogens**...but we pioneer it in bacterial diseases
- **Fast to clinic** & low CMC costs
- Potential to facilitate **multi-component vaccines**



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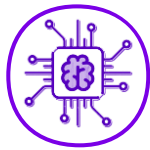
Sanofi's Investments in the mRNA Platform

-

Sanofi establishes a comprehensive *End-to-End mRNA Centre of Excellence* Accelerated by the Acquisition of Translate Bio/USA

Integrated in mRNA CoE

**Driven by the Therapeutic Areas
with robust interface**



**RNA & LNP
Research**

CMC

Automation

**Data
Sciences**

Manufacturing

Programs

**Translational
Science**

**Antigen
design**

A global team with
**>500 CoE
scientists &
engineers**

2 main hubs in the
USA & France

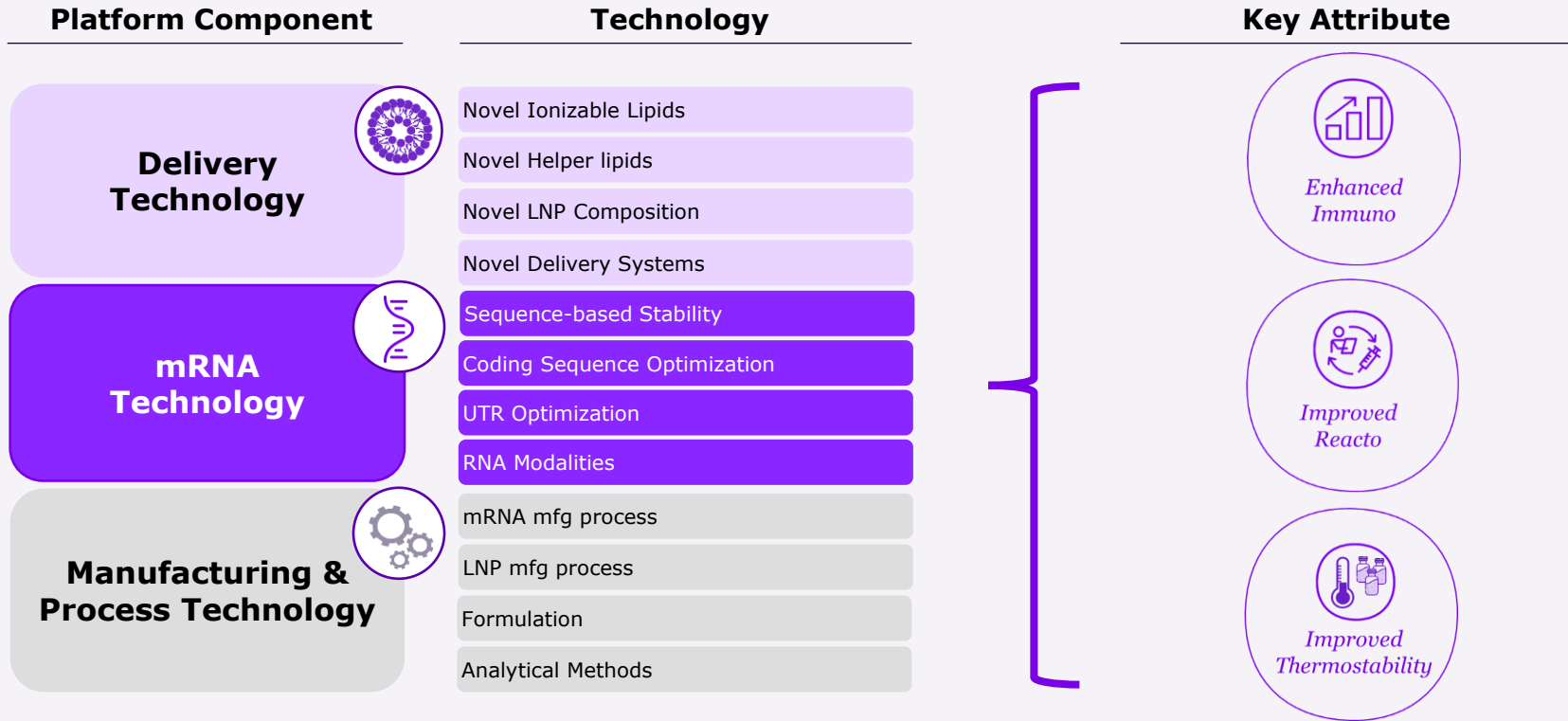
+2 satellites
(FL/USA,
QLD/Australia)

>15 Clinical Trials
Initiated to Date

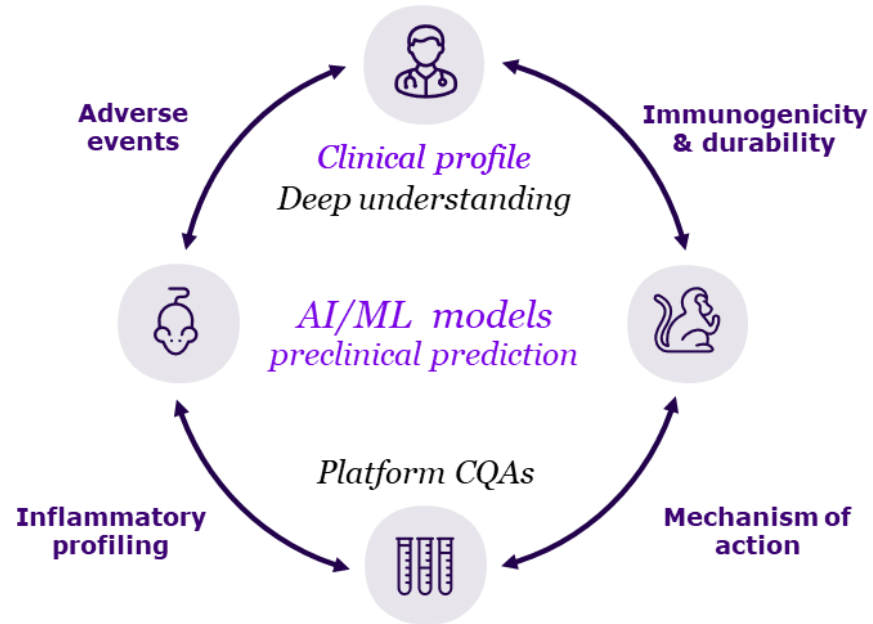
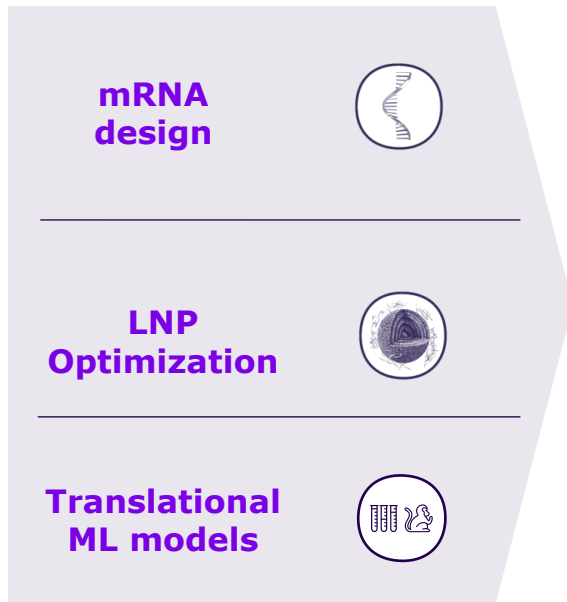
Building the *next generation mRNA* technology for vaccines & other therapeutic areas

	<i>1st gen mRNA</i>	<i>2nd gen mRNA</i>	<i>3rd gen mRNA</i>
Immunogenicity	✓ High	✓ High	✓ High
Reactogenicity	– Moderate to high	✓ Tolerability profile in line with established vaccines	✓ Tolerability profile in line with established vaccines
Thermostability	– ~1 month shelf life (2-8°C)	✓ Lyophilized or 9 – 12 months liquid	✓ Lyophilized or 9 – 12 months liquid
Duration of expression	– 1 – 3 days	– 1 – 3 days	✓ Extended half-life
Targeting	– -	– -	✓ Efficient cell & organ specificity
	Applicable to pandemic market	Required profile for general vaccine markets	Optimal profile for therapeutics

mRNA Vaccine Platform is *defined by 3 components* - key attributes for overall platform success vs traditional modalities



We leverage computational sciences and *AI/ML models*, to accelerate learnings and improve mRNA platform



Sanofi's Interest in External mRNA Innovations



- Improved durability
- Immunomodulators
- Improve antigen presentation (e.g., NP)
- Novel delivery
- mRNA sequence optimization



- Mechanism-based silencing
- Novel delivery
- Dose-sparing strategies



- Formulation dev
- Novel excipients
- Novel delivery
- mRNA sequence optimization



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Influenza



Sanofi is the *Global Leader in Influenza Vaccines*

Pioneered the transition to quadrivalent flu vaccines

Worldwide market leader with €2.7bn sales in 2023

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*



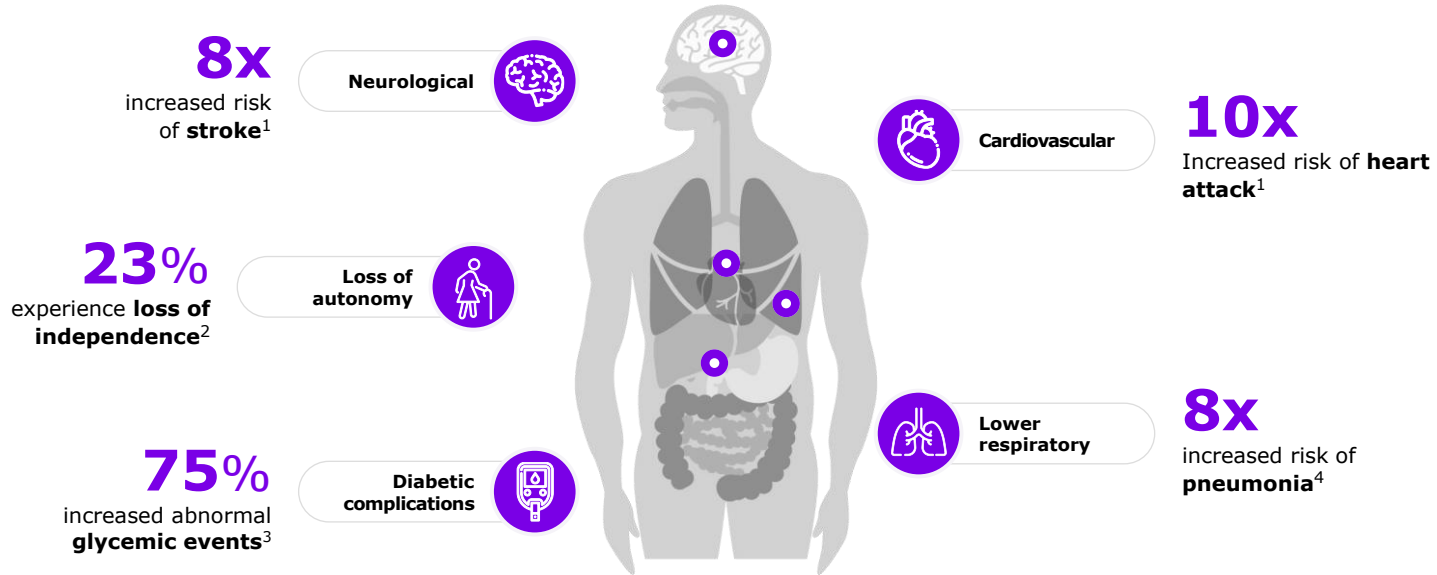
FLU X COVID-19

novavax

May 10, 2024

Protection beyond Flu

Flu an unpredictable virus, with devastating impact on patient lives






WORLDWIDE

3-5M severe cases, **290k-690k** respiratory deaths

US

\$11.2B in annual costs

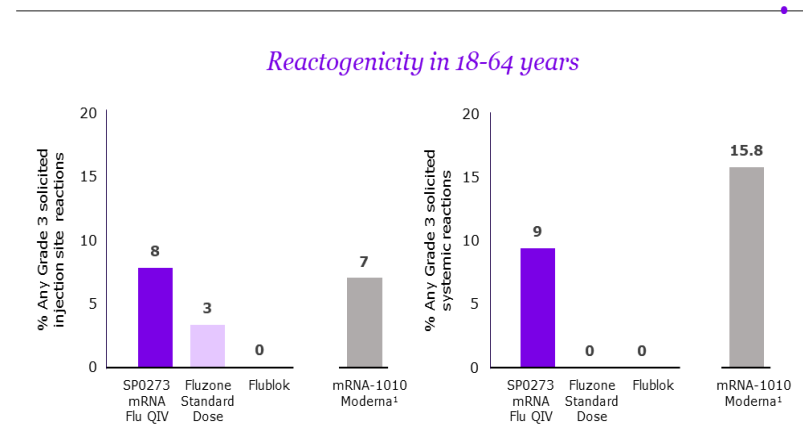
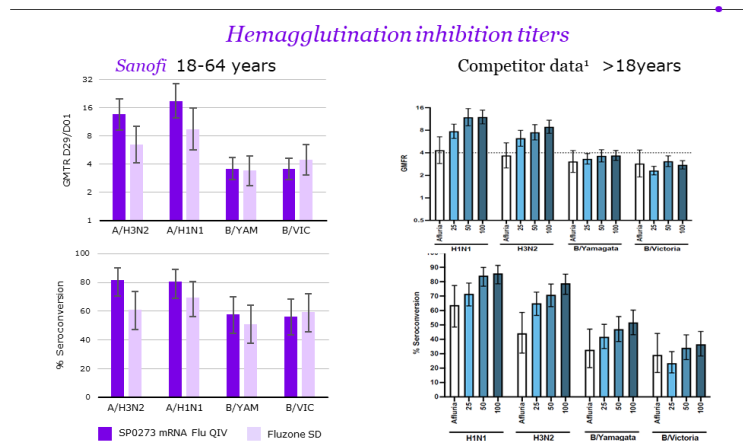
Three attributes imperative for winning in seasonal flu

 Protection Beyond Flu	Demonstrated efficacy in hospitalization and infection reduction through high quality / consistent data – not just immunogenicity
 Safety & tolerability	Excellent tolerability profile
 Administration	Fully liquid formulation, pre-filled syringe Shelf life covering duration of flu season at refrigerator temperature (2-8°C)

Our mRNA influenza vaccine is in the race

Immune response in line with other mRNA flu vaccine program

SP0273 *reactogenicity* compares favorably to other mRNA trial



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.



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RSV



RSV causes severe disease across ages



Beyfortus

Best-in-Class immunization (mAb) for All Infant Protection in first season



RSV Toddler

First-in-Class intranasal live-attenuated vaccine for protection from second season onwards



RSV Older Adult


First-in-Class RSV-hMPV±PIV mRNA combination

Partnership with AstraZeneca 

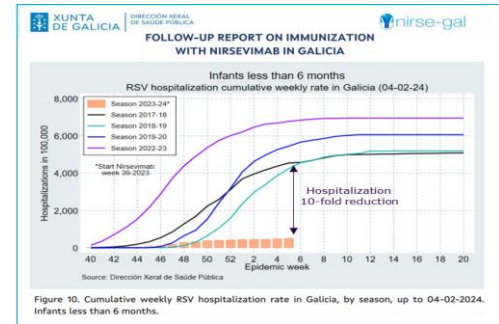
Partnership/Licenses from the 

Beyfortus has consistently delivered strong profile



 designed to *Protect All Infants* => single dose offering protection through the whole season

- *Strong efficacy* and *safety profile* demonstrated in Ph3 program
 - 79.5% efficacy RSV LRTI
 - 83% efficacy RSV LRTI hospitalization
 - Reduction by ~30% of all pediatric hospitalizations
 - Safety profile comparable to placebo
- *Strong real world effectiveness* data from first year implementation
 - Spain & US data demonstrates a 10-fold reduction of RSV hospitalizations
 - In the first season, ~40,000 hospitalizations avoided for families in Spain only



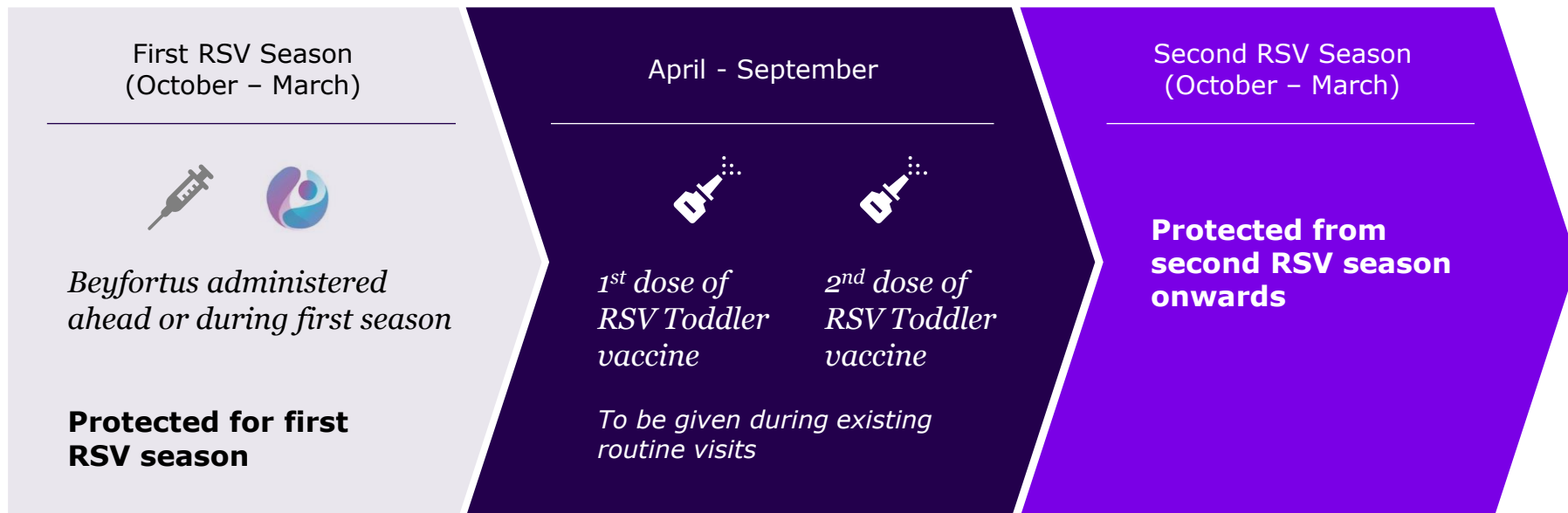
Nirsevimab was 90% effective at protecting infants from RSV-associated hospitalization*

Clinicians, talk to parents about nirsevimab, a preventive antibody

*Estimates from the Real-World Surveillance Network, October 2023-February 2024

MMWR

RSV Toddler vaccine to provide continued protection





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:¹⁻⁶

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

> Limited antigenic drift of RSV, hMPV and PIV *removes need for annual vaccination*⁸

> Sanofi is developing an **mRNA-Based RSV+hMPV** combination vaccine

1. Widmer et al., 2012; 2. Russell et al., 2019 (62% of RSV); 3. Colosia et al., 2017; 4. Using RSV rate from Colosia 2017 as proxy. 5. <https://www.cdc.gov/rsv/research/us-surveillance.html> 6. Compiled data from CDC, 9 seasons from 2010-2011 to 2018-2019 <https://www.cdc.gov/flu/about/burden/index.html> 7. Burden in already vaccinated pop 8. Assuming vaccine durability >1 year



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Pioneering new fields

- ExPEC Vaccine
- Acne Vaccine
- Chlamydia Vaccine

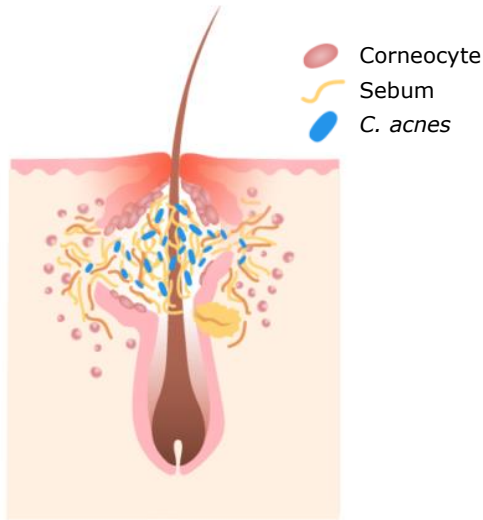


Sanofi Acne vaccine targets a bacteria driving inflammation

- Acquisition of ORIGIMM, Austria

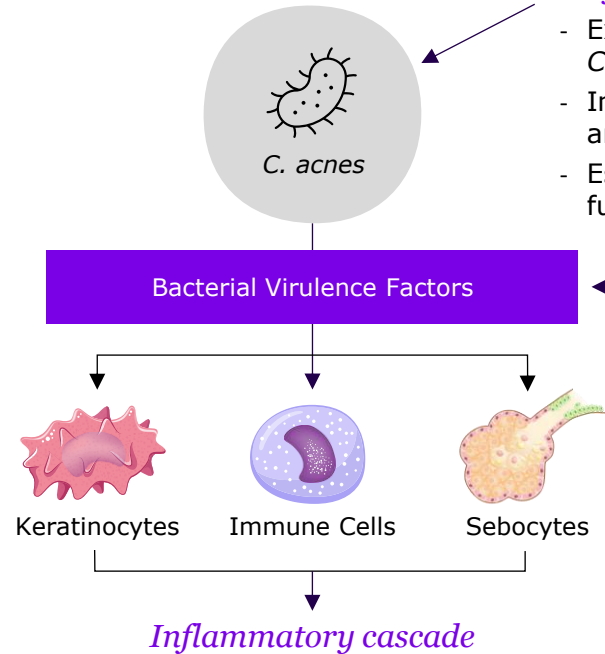


Acne vulgarum: skin dysbiosis driven by outgrowth of pathogenic *Cutibacterium acnes*



Origimm Antigens

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



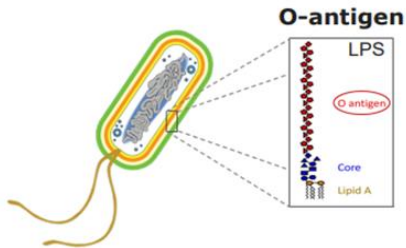
Additional Vaccine Antigen

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

Pharmaceutics 2019, 11(10), 490; <https://doi.org/10.3390/pharmaceutics11100490> Targeted Topical Delivery of Retinoids in the Management of Acne Vulgaris: Current Formulations and Novel Delivery Systems by Gemma Latter

E. coli-related Sepsis vaccine (ExPEC) – Partnership with J&J

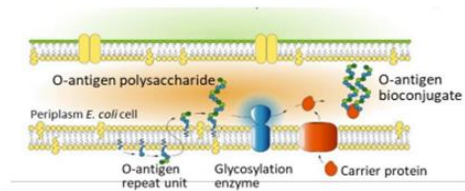
Antigen target and prevalence



- Highly immunogenic surface structures
- Inducing opsonophagocytic protective antibodies
- Most prevalent 9 O-antigen serotypes, out of >180 O-serotypes

Technology

In vivo bioconjugation



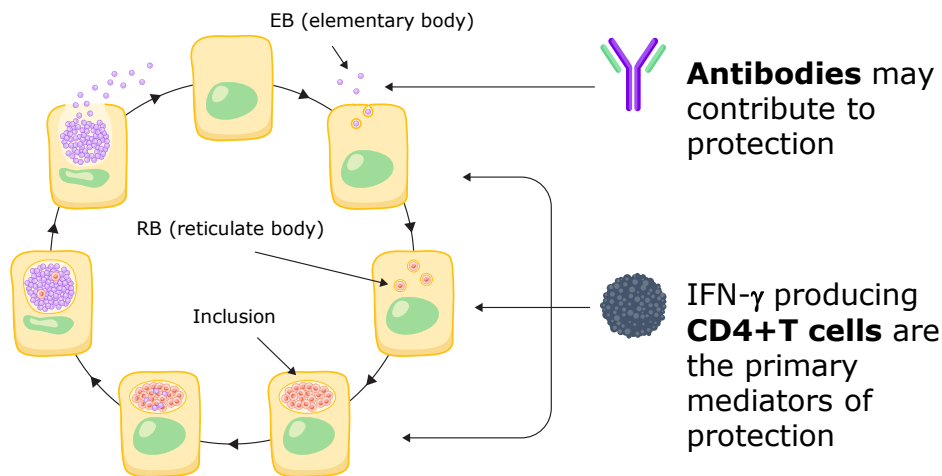
- In-licensed bioconjugation technology developed by GlycoVaxyn AG
- Enables manufacturing of glycoconjugates *in vivo* using engineered *E. coli*

- ExPEC is a **leading cause of sepsis**
- *E. coli* is one of the bacteria ranked as highest **antimicrobial resistance** threat by WHO & CDC
- **Phase 3 clinical trial** ongoing; target 18,000 volunteers; recruitment >50%

Comprehensive Chlamydia vaccine candidate to address the bacteria's complex biology



Chlamydia trachomatis (CT) is a bacterium that lives inside human cells



Targeted immune profile

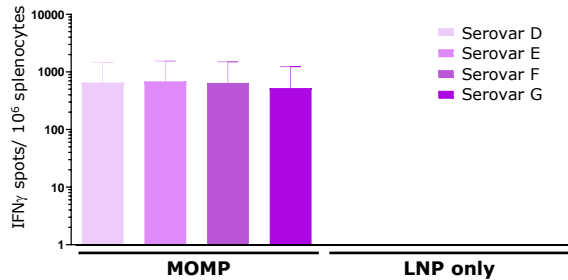


- **Antibodies and CD4 T cell** responses
- **Recognition of multiple chlamydia serovars (serotypes)**
- **Broad population coverage** (HLA: Human Lymphocyte Antigen)

Innovative multi-antigen vaccine candidate achieves targeted immune profile

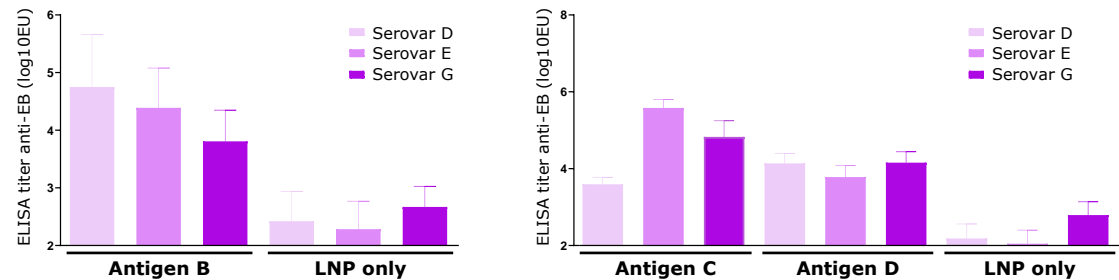


Broad cross-serovar T cell responses



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

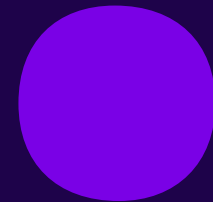
Cross-serovar antibodies recognizing *Chlamydia trachomatis* Elementary Bodies (EBs)





















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




Multi-antigen vaccine candidate elicits cross serovar IFN- γ producing T cells and EB binding antibodies

Sanofi Collaborative Programs & Partnerships



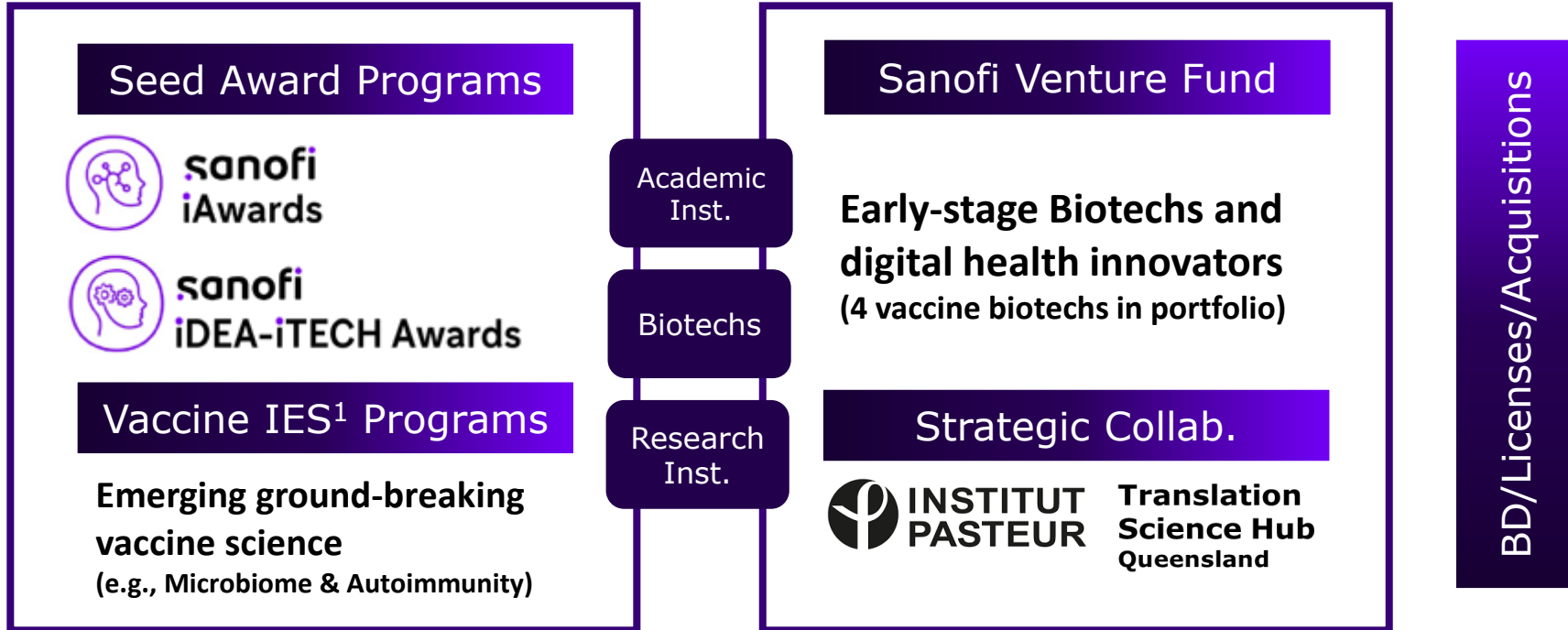
Sanofi Vaccines has a Long History of Public Private Partnerships

	 	 	  	 
Project	Pandemic Preparedness	BioMed Sci Ecosystem	EVF & mRNA	BioMed Sci Ecosystem
Objective	Vaccine supplies for US (Pandemic Flu, CoV)	Sci. Consortia Creation	R&D and manufacturing	mRNA platform, Chlamydia vaccine
Funding Mechanism	100% USG-funded Contracts	50-50 Private/Public Co-funding	Private/Public Co-funding	Private/Public Co-funding
Dates	2004-present	2015-2024	2022-present	2023-present
Scope	  		  	 

 Research
  Manufacturing (Commercial scale)
 Development

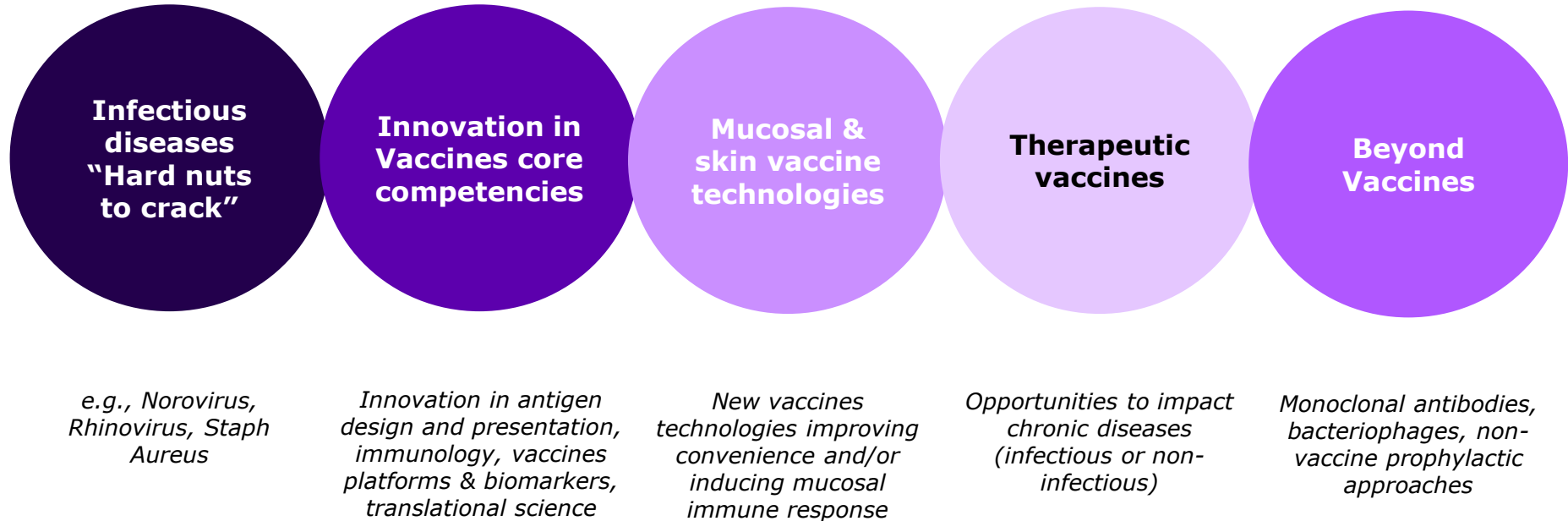
Sanofi Vaccines: R&D Partnership Mechanisms

Open Innovation



¹IES, Innovation and Emerging Sciences

Next wave of Innovation - Fields of major interest



next level of seed awards ...



Immune-based, antigen-specific solutions for
autoimmune diseases, neurological diseases, and
dyslipidemia
2025

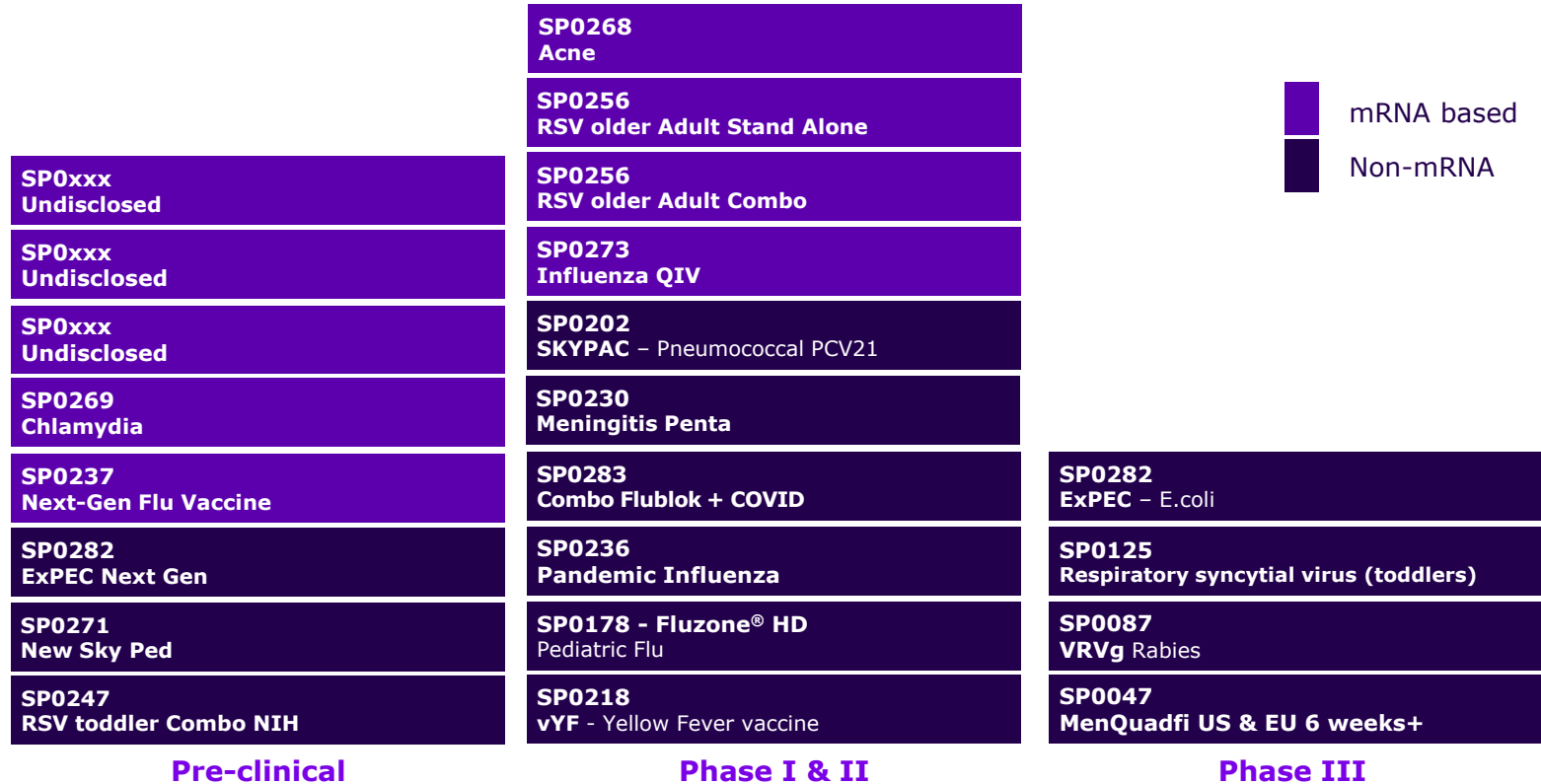
Up to 500k USD grant

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Conclusion

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We are building an industry leading vaccine pipeline



Bringing External Innovation is a key success factor for Sanofi Vaccines

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Thank you
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