Pfizer

Preparing for A/H5N1

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Possible Advantages of mRNA Vaccine Platform Led to Initiation of Pfizer's Influenza Program in 2018

Safety

Non-infectious, chemically defined, no viral foreign proteins

Rapid Response

Technology may enable **rapid development** and **quick production scaling**

Efficacy?

Preclinical/early clinical work: **Broad immune responses**, both antibodies and T-cells

August 18, 2018 –License Agreement from BioNTech for Pfizer to Develop mRNA-based Vaccines for Prevention of Seasonal Influenza

Traditional Flu Vaccines Timeline Require Longer Lead Time

mRNA Platform Shortens Timelines Which Could Enable a Quicker Response to Flu Evolution

mRNA Platform Could Allow for the Future Opportunity to Move Strain Selection From 6 Months Prior to Vaccination to as Little as 3 Months

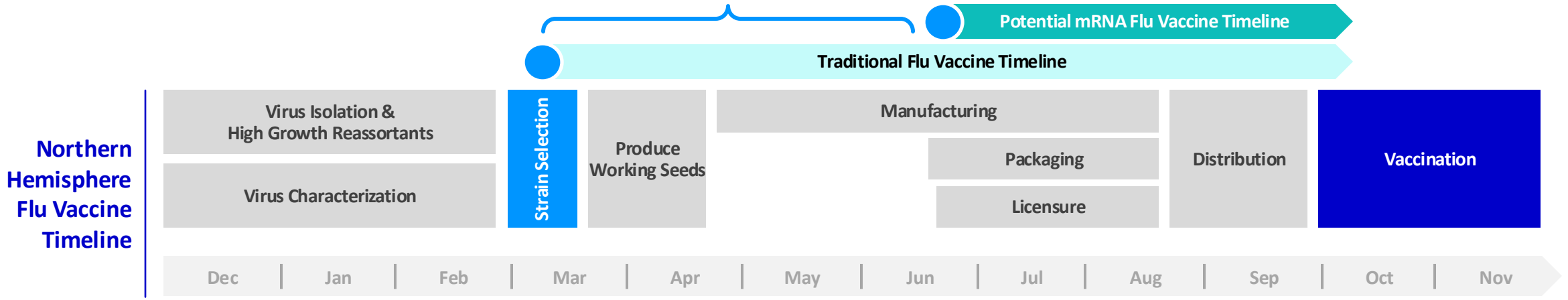


Figure modified from Weir and Gruber, *Influenza Other Respir Viruses*. 2016 Sep; 10(5): 354–360.

The Global Impact of COMIRNATY® Showcases the Potential of a Pfizer mRNA Influenza Vaccine

Population Impact[1]

~4.5 B doses of COMIRNATY® (COVID-19 Vaccine, mRNA) have been shipped since 2020

All In House End-to-End Vaccine Capabilities

Vaccine R+D

Supply + Manufacturing

Global Vaccines Distribution

Global Reach

183 countries and territories have received doses of COMIRNATY® (COVID-19 Vaccine, mRNA) since 2020

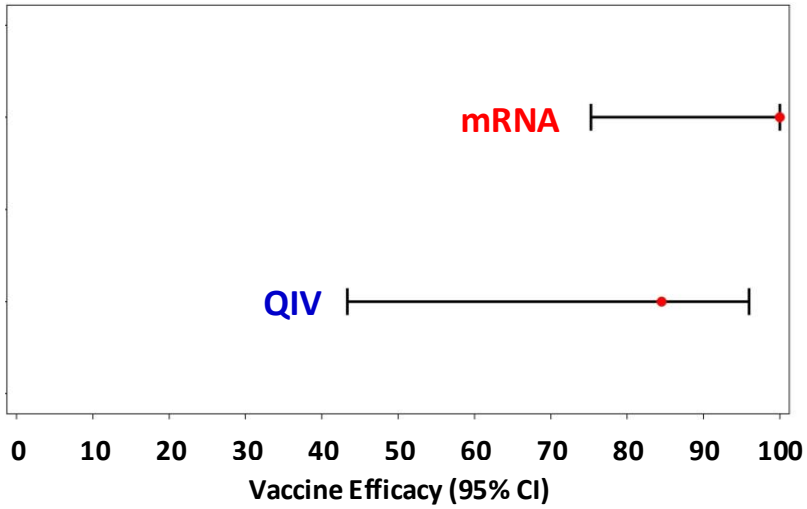
1. CDC, ECDC, OWID, Country Websites, Pfizer Assessment.

mRNA vaccines induced HAI titers associated w/ reduction in viral shedding and protection against virus in a human challenge study (Sponsor: hVIVO Services Limited; ISRCTN13789612)

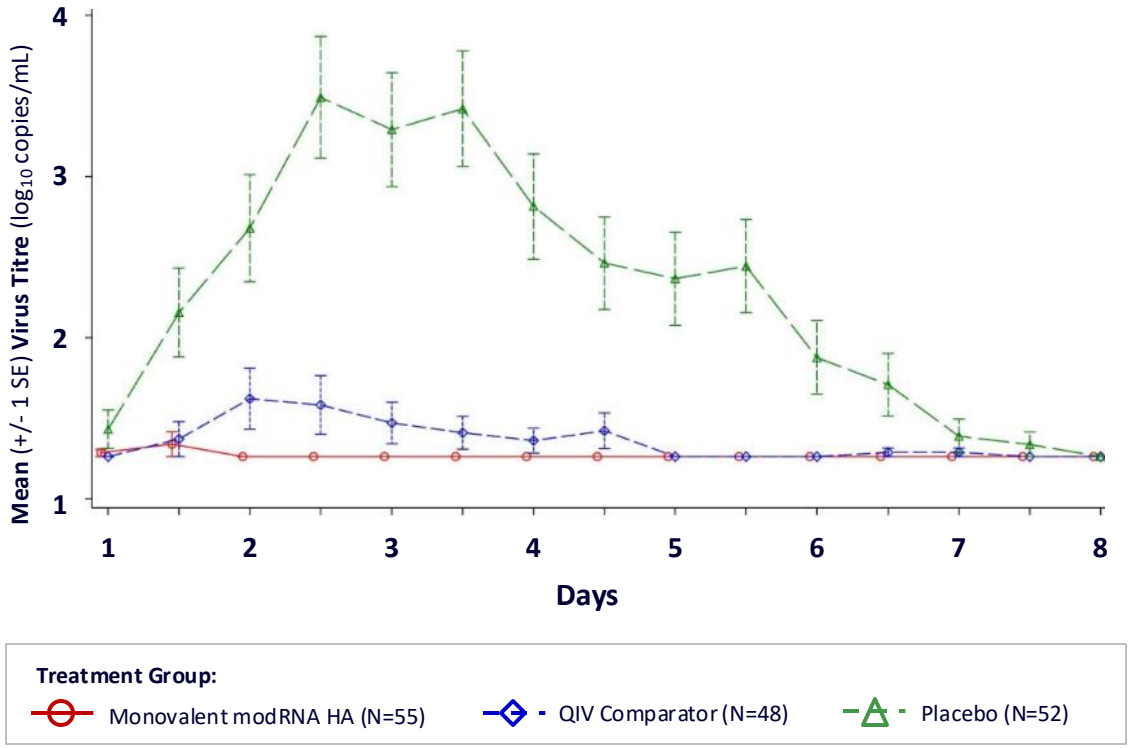
	Monovalent mRNA HA (95% CI) (N=73)	QIV (95% CI) (N=73)	Placebo (95% CI) (N=44)
Post-Vx Seroconversion	**97%** (89.63, 99.64)	**92.6%** (83.67, 97.57)	N/A
Post-Vx Seroprotection*	**100%** (94.94, 100.00)	**94.1%** (85.62, 98.37)	**13.6%** (5.17, 27.35)

*Seroprotection defined as HAI titer ≥ 1:40

Forest Plot of Vaccine Efficacy for qRT-PCR Confirmed Moderately Severe Influenza Infections



Mean Influenza Challenge Virus Load by qRT-PCR



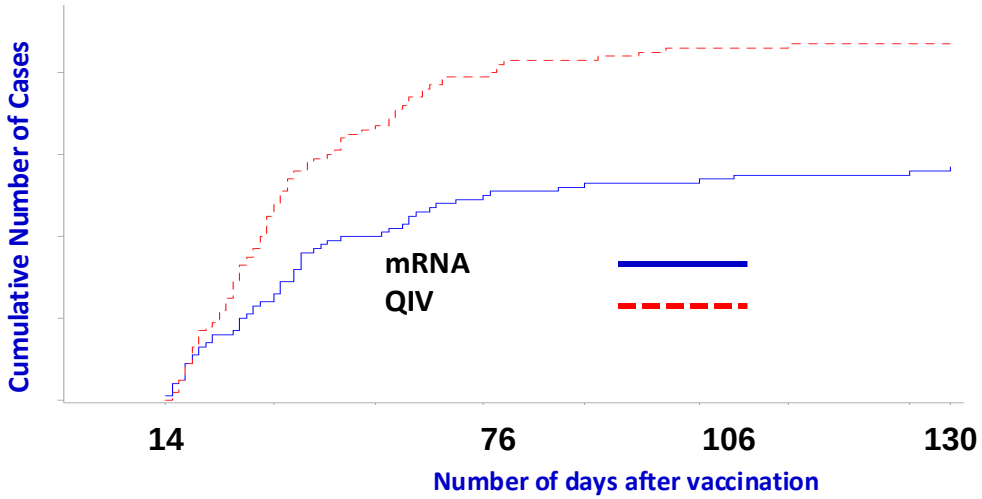
mRNA Flu Phase 3 in 18-64 Years Old Met Primary Efficacy Objectives (NI & Superiority) During a Season Dominated By Flu A Cases (NCT05540522)

Phase 3 Study Demonstrated Efficacy and Immunogenicity of mRNA Flu

- **18- to 64-year-old participants (N= 18,607)**
  - –Randomized 1:1 for comparison against licensed standard dose (QIV)
  - –NH 2022/3 Influenza Season (conducted in the US)
- **Primary Objectives:**
  - –Non-inferior Efficacy vs QIV: **MET**
  - –Superior Efficacy vs. QIV: **MET**
  - –Safety: similar overall safety profile vs QIV, some increase in mild/moderate reactogenicity
- **Secondary Objectives:**
  - –Non-inferior Immunogenicity (A influenza strains): **MET**
  - –Non-inferior Immunogenicity (B influenza strains): **NOT MET**

Flu Cases: A Influenza; Immune responses mirror efficacy trend (A strain dominant)

Laboratory-Confirmed Influenza Case Accruals 18 to 64 Yr, Efficacy Evaluable Population

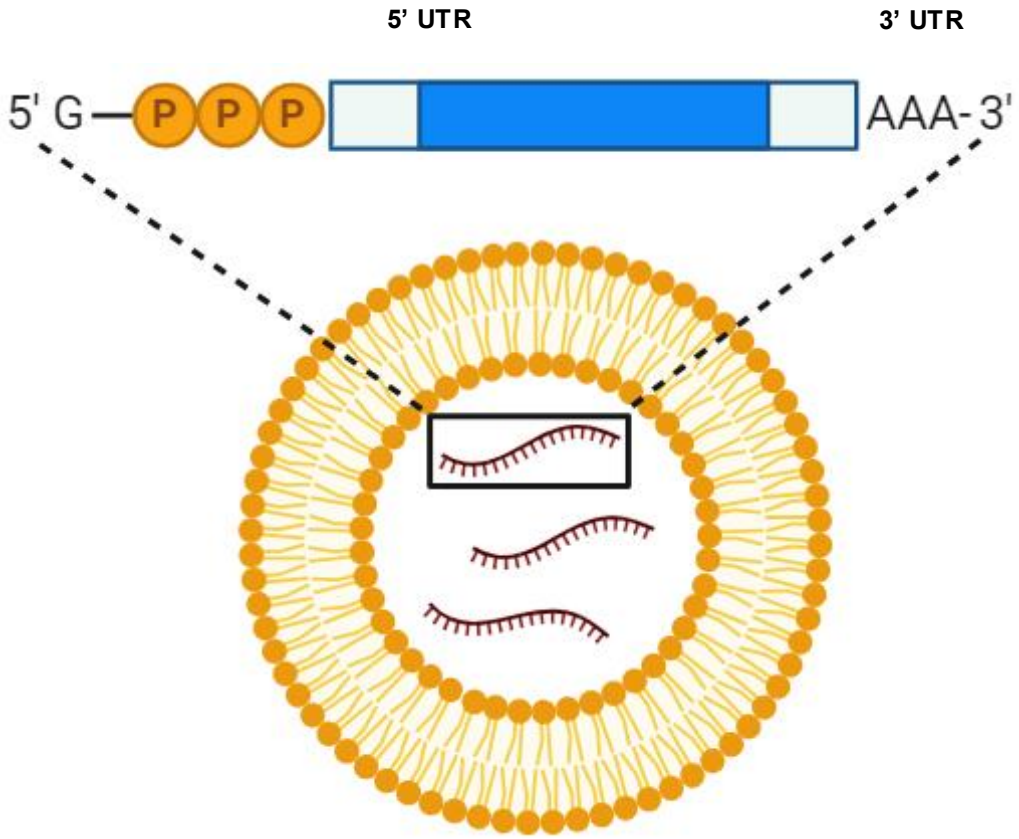


Immune Responses

	GMTr NI (Assay 1)	SCR diff NI (Assay 1)	GMTr NI (Assay 2)	SCR diff NI (Assay 2)
A/H3N2	+	+	+	+
A/H1N1	+	+	+	+
B/Yamagata	-	-	+	+
B/Victoria	-	-	-	-

Pfizer's pre-pandemic influenza vaccine (pdmFlu)

Target Indication: Active immunization for the prevention of disease caused by the influenza A virus H5 HA subtype encoded by the vaccine for use in individuals 6 months of age and older

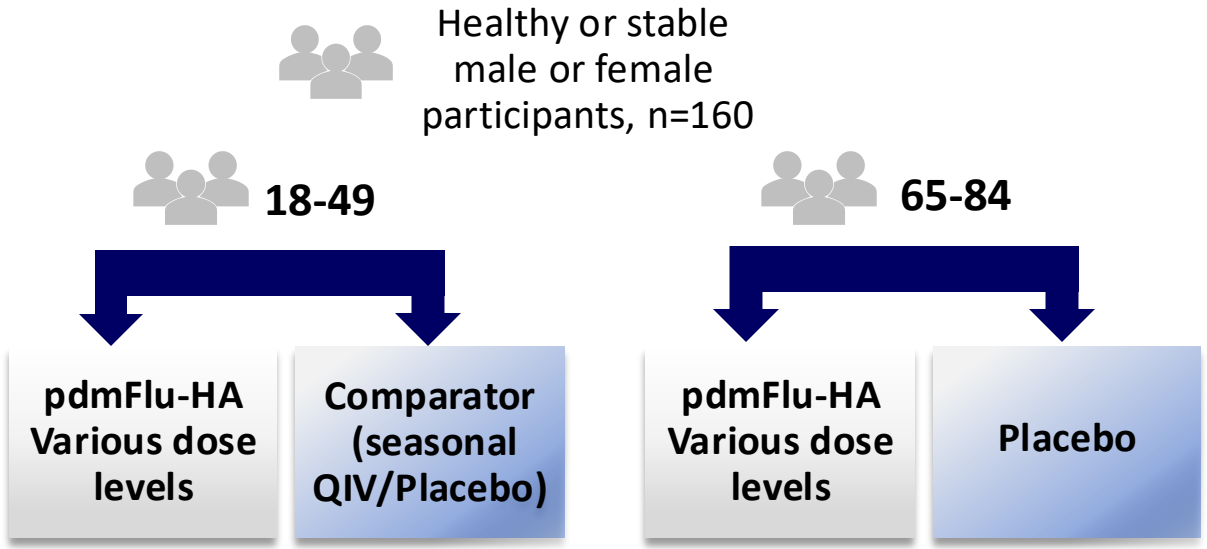


- pdmFlu encodes for influenza HA from A/Astrakhan/3212/2020 (H5N8) from H5 clade 2.3.4.4b
- Same nucleoside-modified mRNA and lipid nanoparticle delivery technology as Comirnaty and investigational seasonal mRNA Flu vaccines
- pdmFlu elicited robust dose-dependent antibody and cell-mediated immune responses in mice

pdmFlu is under evaluation in a First-in-Human Phase 1 Clinical Trial

Objective: To identify one or more doses of pdmFLU with acceptable immune response and safety profile in healthy adults

Study Design



Key Endpoints

Primary

- Safety/tolerability, safety laboratory assessments

Secondary

- Immunogenicity

ClinicalTrials.gov identifier: NCT06179446

Thank You