Overview: Influenza Vaccines in Development

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NAIIS Flu Day
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**Agenda**

- New seasonal / pandemic vaccines
- Universal influenza vaccines
- Influenza monoclonal antibodies (mAbs)
**Overarching considerations**

- Focus primarily on vaccines in clinical trials in humans (Phase I-III) and less so pre-clinical development (animal data)
- Data sources:
  - Bio MedTracker subscription data base [www.biomedtracker.com](http://www.biomedtracker.com)
  - Press releases, websites and publications by vaccine developers
  - Published articles on general vaccine development

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New seasonal flu vaccines
New vaccines leverage faster technologies that could also boost the vaccine immune response

- New technologies being utilized:
  - Cell
  - Recombinant
    - VLP
    - Plant-based
    - Oral tablet
    - Nasal
  - Novel adjuvants
  - mRNA
- Many candidates have data on both seasonal and pandemic strains
- Many companies plan to combine Influenza and COVID-19

### Novel Vaccines in Later Stage Development

<table>
<thead>
<tr>
<th>Phase</th>
<th>Company</th>
<th>Technology</th>
<th>Population(s)</th>
<th>Compared to</th>
<th>Key results</th>
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</thead>
<tbody>
<tr>
<td>Phase III</td>
<td><strong>Medicago</strong></td>
<td>Recombinant, plant-based quadrivalent VLP (injection)</td>
<td>Adults 18-64; Adults 65+</td>
<td>Placebo; QIV vaccine</td>
<td>18-64: did not meet primary endpoint 65+: demonstrated non-inferiority Generally well tolerated</td>
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<tr>
<td>Phase III</td>
<td><strong>Novavax</strong></td>
<td>Recombinant quadrivalent nanoparticle with Matrix-M adjuvant (injection)</td>
<td>Older adults</td>
<td>Fluzone QIV</td>
<td>Achieved primary endpoints for efficacy; demonstrated antigen-specific CD4+ T cell immunity Generally well tolerated</td>
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<tr>
<td>Phase II</td>
<td><strong>Seqirus</strong></td>
<td>Cell-based quadrivalent with MF-59 adjuvant (injection)</td>
<td>Adults 50 and over</td>
<td>None: 8-arm dose ranging</td>
<td>Results not yet published: Phase II ongoing with Phase III planned for 2H2022</td>
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<tr>
<td>Phase II</td>
<td><strong>Vaxart</strong></td>
<td>Recombinant oral tablet</td>
<td>Older adults</td>
<td>Double blind; Fluzone QIV</td>
<td>Human challenge model study; Single tablet provided efficacy (reduction in disease and infection rates);</td>
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<td></td>
<td><strong>Sanofi</strong></td>
<td>Fluzone HD pediatric</td>
<td>Children 6-35 months old</td>
<td>Standard QIV</td>
<td>Enrollment underway</td>
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Numerous companies are pursuing mRNA for influenza vaccines

- Several mRNA and self-amplifying mRNA vaccines are in Phase I / II trials
  - Moderna - multiple Phase I and II trials of both seasonal and potentially pandemic strains; studies designed to demonstrate safety, tolerability and immunogenicity (some compared to current vaccines).
  - Pfizer – announced a randomized Phase 1 study of safety, efficacy and tolerability of vaccine made with dominant seasonal strains
  - Sanofi – Initial data show potential benefit of mRNA vaccine at various doses; plan to initiate Phase I modified mRNA monovalent trial 1H2022 and quadrivalent in second half of 2022
  - Seqirus – plan to initiate Phase I trials for self-amplifying mRNA seasonal and pandemic vaccines in 2H2022

Universal flu vaccines
Universal influenza vaccines are progressing through clinical trials

FluGen

- A New Approach: M2SR = M2 Deleted Single Replication Live Virus Vaccine
- Supra-seasonal and intranasal one dose vaccine
- Published, randomized, placebo-controlled, human challenge, Phase II trial in adults 18-64 years against highly drifted H3N2 virus
- Subjects produced vaccine-induced neutralizing antibodies that were protective against infection and illness after being challenged with a highly drifted strain of H3N2
- Vaccine was generally well tolerated

Universal influenza vaccines are progressing through clinical trials

IMUTEX

- Broad spectrum “Universal” Flu vaccine that targets conserved internal proteins common to all influenza viruses
- Adjuvanted one dose or two dose vaccine
- Study 1 - Published randomized, placebo-controlled Phase II trial in adults 18-60 years
  - Subjects produced vaccine-induced neutralizing antibodies that were statistically higher than placebo
- Study 2 - Published randomized, placebo-controlled, human challenge Phase II study in adults 18-55 years; intranasal challenge of H1N1 with a primary endpoint of mild / moderate influenza disease
  - Both vaccine groups experienced significantly lower disease symptoms compared to the placebo group
- Vaccine was generally well tolerated in both studies
Universal influenza vaccines are progressing through clinical trials

Vivaldi Biosciences

- Self-adjuvanting vaccine
- Immunized volunteers generated antibodies with broad cross-neutralizing activities in the nasal passages and blood serum against unmatched influenza strains.
- A comparison of Phase 1 results showed a superior immune response achieved versus other vaccine approaches for protection against influenza H5N1. After a single dose, 75% of volunteers achieved seroconversion (a key measure of antibody response) while other vaccine approaches, including adjuvanted vaccines, achieved just 5% to 58% seroconversion.
- Vaccine was generally well tolerated in both studies
**Long-acting monoclonal antibodies offer a potential option to preventive vaccines**

**Vir**
- VIR-2482 is a fully human immunoglobulin G1 mAb directed against a highly conserved epitope in the influenza A hemagglutinin stem region for prevention of influenza A illness.
- Phase I conclusions show that, following a single IM dose in health subjects, VIR-2482 has been well tolerated at doses up to 1800 mg and maintained systemic exposure for greater than/equal to 20 weeks.
- The preliminary pharmacokinetic data demonstrates potential for once-per-season dosing.
- Overall, first-in-human data support initiation of Phase II study to evaluate efficacy.
- Preclinical data show that VIR-2482 has broad binding and neutralizing potential against all major strains of influenza A, including pandemic strains, from the last 100 years.
- VIR-2482 administered prophylactically 24 hours prior to lethal doses of influenza significantly reduced morbidity and prevented mortality in mouse models.

**NIAID**
- Researching other mAbs against various influenza types

Questions?