The Road to Immunity During COVID-19: Developing & Distributing a Vaccine

NAM-APHA COVID-19 Conversations Webinar
10 June 2020

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CEO, CEPI
Our mission

CEPI accelerates development of vaccines against emerging infectious diseases and enables equitable access to these vaccines for affected populations during outbreaks.
Disease X: COVID–19

As of 9 June

7.1m Confirmed cases

406,807 Deaths

188 Countries

The spread of COVID-19 has become a humanitarian and economic crisis, unprecedented in modern times.
Global Snapshot of COVID-19 Vaccine Development
Covid-19 vaccine R&D landscape

- **Exploratory**: project has not started with in-vivo testing
- **Preclinical**: project started to test in-vivo / manufacture CTM but not yet started with testing on human
- **Phase I**: safety and immunogenicity; **Phase IIa**: Safety and efficacy and dose schedule; **Phase I/II**: combine of Phase I and IIa. Start is defined as first subject dosed
- **Unconfirmed**: the development status cannot be confirmed using available internal and publicly available information
Current CEPI COVID-19 vaccine portfolio consists of 9 projects:

<table>
<thead>
<tr>
<th>Inovio</th>
<th>University of Queensland / CSL</th>
<th>CureVac</th>
<th>Moderna</th>
<th>Clover BioPharma</th>
<th>Merck / Themis</th>
<th>Novavax</th>
<th>University of Hong Kong</th>
<th>AZ / Univ. Oxford</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Platform</td>
<td>Antigen / Adjuvant</td>
<td>Current phase</td>
<td></td>
<td></td>
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<tr>
<td>USA</td>
<td>DNA</td>
<td>Full-length S protein</td>
<td>Phase 1</td>
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<tr>
<td>Australia</td>
<td>Protein</td>
<td>Full-length S protein / MF59 or AS03 or CPG1018</td>
<td>Preclinical</td>
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<tr>
<td>Germany</td>
<td>RNA</td>
<td>Full-length S protein</td>
<td>Preclinical</td>
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<tr>
<td>USA</td>
<td>mRNA</td>
<td>Full-length S protein</td>
<td>Phase I1a</td>
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<tr>
<td>China</td>
<td>Protein</td>
<td>Full-length S protein / AS03 or CPG1018</td>
<td>Preclinical</td>
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<tr>
<td>USA/Austria</td>
<td>Protein</td>
<td>Full-length S protein</td>
<td>Preclinical</td>
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<tr>
<td>USA</td>
<td>Protein</td>
<td>Full-length S protein / saponin-based Matrix-M</td>
<td>Preclinical</td>
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<tr>
<td>China</td>
<td>Viral Vector</td>
<td>Receptor Binding Domain / AS03</td>
<td>Preclinical</td>
<td></td>
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<tr>
<td>UK</td>
<td>Viral Vector</td>
<td>Full-length S protein</td>
<td>Phase I/II</td>
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**Adjuvants**
- Dynavax
- Seqirus

**Speed**

**Scale**

**Access**
11 Covid-19 vaccine candidates in clinical trials

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Vaccine characteristics</th>
<th>Current stage</th>
<th>#Sites/Location</th>
<th>Lead Partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad5-nCoV</td>
<td>Adenovirus type 5 vector that expresses S protein</td>
<td>Phase I/II</td>
<td>? sites / China</td>
<td>Cansino</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Inactivated Novel Coronavirus Pneumonia vaccine (Vero cells)</td>
<td>Phase I/II</td>
<td>? sites / China</td>
<td>Wuhan Institute of biological products</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Inactivated novel coronavirus (2019-CoV) vaccine (Vero cells)</td>
<td>Phase I/II</td>
<td>1 site / China</td>
<td>Beijing Institute of Biotechnology</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Inactivated SARS-CoV-2 inactivated vaccine</td>
<td>Phase I/II</td>
<td>1 site / China</td>
<td>Sinovac Biotech</td>
</tr>
<tr>
<td>ChAdOx1</td>
<td>ChAdOx1 vector that expresses S protein</td>
<td>Phase I/II</td>
<td>6 sites / UK</td>
<td>AZ / Oxford</td>
</tr>
<tr>
<td>nCoV-19</td>
<td>DCs modified with lentiviral vector expressing synthetic minigene based on domains of</td>
<td>Phase I/II</td>
<td>3 sites / China</td>
<td>Shenzhen GIMI</td>
</tr>
<tr>
<td>LV-SMENP-DC</td>
<td>selected viral proteins; administered with antigen-specific CTLs</td>
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<tr>
<td>mRNA-BNT162</td>
<td>mRNA NRM / SAM constructs with LNP</td>
<td>Phase I/II</td>
<td>1 site / Germany</td>
<td>Pfizer; BioNTech</td>
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<tr>
<td>NVX-CoV2373</td>
<td>stable, prefusion protein, includes Matrix-M™ adjuvant</td>
<td>Phase I/II</td>
<td>7 sites / US</td>
<td>Novavax</td>
</tr>
<tr>
<td>Pathogen-specific aAPC</td>
<td>aAPCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins</td>
<td>Phase I</td>
<td>2 sites / Australia</td>
<td>Novavax</td>
</tr>
<tr>
<td>mRNA-1273</td>
<td>LNP-encapsulated mRNA vaccine encoding S protein</td>
<td>Phase I/II</td>
<td>10 sites / USA</td>
<td>Moderna Therapeutics</td>
</tr>
<tr>
<td>INO-4800</td>
<td>DNA plasmid encoding S protein delivered by electroporation</td>
<td>Phase I</td>
<td>2 sites / USA</td>
<td>Inovio Pharmaceuticals</td>
</tr>
</tbody>
</table>
Clinical development is proceeding at unprecedented speed

- 11 January 2020 - genetic sequence of SARS-CoV-2 published
- 11 May 2020 – Moderna mRNA-1273 enters Phase II
- 1 April 2020 – first Covid-19 vaccine candidate reported to enter Phase II (Cansino Ad5-nCoV)
- 3 June 2020 – 11 Covid-19 vaccine candidates in clinical development
- Several developers have indicated targets for doses to be available from late 2020, early 2021
- 8 April 2020 – 5 Covid-19 vaccine candidates in clinical development
- 16 March 2020 – first Covid-19 vaccine candidate enters Phase I (Moderna mRNA-1273)
- 22 May 2020 – AstraZeneca announce opening of recruitment for Phase II / III trial

Compared with:
- *Ebola* – 5 years
- *Pandemic Influenza* – 7 years
- *HBV* – 16 years
>60 vaccines will enter clinical development by the end of 2020
Speed requires a paradigm shift

**Traditional paradigm**
5 – 10+ years

- Target ID, development partner selection, and pre clinical
  6-36 months
- Phase I
  6-24 months
- Phase IIa
  6-12 months
- Phase IIb
  6-12 months
- Phase III
  12-36 months
- Licensure
  3-18 months

**Outbreak paradigm**
12 – 18 months

- Target ID, development partner selection, and pre clinical
  4-8 months
- Go/no-go decision to invest in candidates
- Clinical development
  Early stage
  3-4 months
  Late stage
  6-8 months
  First in human (PhI)
  Late Stage (PhII) development
  n=10s to n=100s
  Advanced development
  n=100s to n=1000s
  Final stage production / (Emergency authorization)

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057755
COVID-19 vaccines are being developed on many platforms

<table>
<thead>
<tr>
<th>Technology platform</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attenuated / inactivated</td>
<td>Relative ease of development; if replicating, may lead to longer lasting response</td>
<td>If non-replicating, requires more frequent boost than live vaccine; generally requires BSL3 / BSL4 manufacturing capability</td>
</tr>
<tr>
<td>Viral vector</td>
<td>High antibody and T-cell response; ability to select optimal antigen; possible for single-dose protection; replicating virus can use a lower dose; higher productivity in manufacturing; reproducible for different pathogens</td>
<td>Relatively long development time to make master virus/release production starting materials; may not be appropriate for immune-compromised patients; may elicit immune response against vector rather than antigen; stability may require low temperature storage or lyophilization</td>
</tr>
<tr>
<td>Recombinant protein / subunit</td>
<td>Ability to select optimal antigen; existing manufacturing capacity / productive platforms / many licensed products with the technology; allows for relatively easy dose optimization</td>
<td>Generally require adjuvant; often process development needed for new targets (platforms that don't change are being developed)</td>
</tr>
<tr>
<td>Virus-like particles</td>
<td>Safe; ability to select optimal antigen; can display antigens from multiple strains; more immunogenic than soluble protein</td>
<td>Likely to require adjuvant</td>
</tr>
<tr>
<td>DNA</td>
<td>Scalable manufacturing process for bulk drug; fast response time to new disease target; flexible for a variety of disease targets (bacterial, viral)</td>
<td>Requires a device that is currently limited in supply and high in cost for LMIC</td>
</tr>
<tr>
<td>RNA</td>
<td>Potential fast response to new disease target; flexible for a variety of disease targets (bacterial, viral);</td>
<td>Delivery requires specialist delivery systems (e.g. LNPs); new technology, so capacity needs to be created (limited existing production capabilities); stability may require low temperature storage or lyophilisation</td>
</tr>
</tbody>
</table>
Concluding thoughts and open questions

• There is no scenario in which vaccines will not be in short supply in 2021
  o The careful management of COVID-19 vaccines as a scarce resource will be essential if we are to end the acute phase of the pandemic and achieve equitable access.

• Many of the Covid-19 vaccine development approaches are high-risk

• Many questions are likely to remain and require longer term follow up, e.g.:
  o Long-term effectiveness / durability of response
  o Long-term safety follow-up
  o Potential for differential responses due to population heterogeneity
  o Breadth of protection against virus mutation or genetic drift / shift

• The first vaccines to market may not be optimal and it will be important to maintain a comprehensive strategic approach for the long term – built on an evolving understanding of disease epidemiology and vaccine effectiveness