Perspectives on navigating a pandemic disruption and advancing competing vaccine development efforts beyond COVID-19

David A. Lindsay, PhD
Directorate Head, Vaccine Clinical Materials Program (VCMP) at Leidos Biomedical Research, Inc.

12 June, 2020

DISCLAIMER: these perspectives are my own and do not necessarily represent the views of Leidos Biomedical Research or Frederick National Laboratory or USG-NIH /NIAID/ VRC.
VCMP vaccine pilot plant activities during COVID-19

- Ensuring continuity of operations
  - Establishing/implementing site-centric business continuity of operations strategy and framework

- Staying the course with competing priorities in a contract environment
  - Pivoting during a transient pause to support the community and local institutes
  - Returning to the workplace

- Supporting COVID-19 vaccine development
  - Assessing the competitive landscape; unique NIAID-VRC industry rapid response effort (mRNA)
  - Planning horizon and VCMP capabilities to support protein-based vaccine advancement
Pandemic “disruption” – how are we doing as an essential business?

Key success elements

• Business continuity framework and gates
• Communications plan (site-specific)
• Cross-functional leadership endorsement
• Enterprise-wide EOC/ emergency Ops committee

Actions/Decisions

• ID of essential /minimal staff and rostering
  – Staff tracker tool implemented on Teams
  – Telework policies extended for all staff w/ HR
• Facility status changes
  – March: A to B (3/17), then to C (3/31)
  – May: return to B status; managing to no more than 50% onsite staff on any given day

4-tier Framework

<table>
<thead>
<tr>
<th>STATUS</th>
<th>Facility Operation</th>
<th>Production</th>
<th>Onsite Staffing Plan</th>
<th>Telework</th>
<th>Site-wide Notification</th>
<th>Risk level</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Normal</td>
<td>Normal</td>
<td>All staff except for routine telework and those on approved leave</td>
<td>Routine</td>
<td>N/A</td>
<td>Low</td>
</tr>
<tr>
<td>B</td>
<td>Normal</td>
<td>Normal</td>
<td>Minimal # of staff to maintain normal operations</td>
<td>Non-routine</td>
<td>YES</td>
<td>Moderate</td>
</tr>
<tr>
<td>C</td>
<td>Reduced</td>
<td>Paused</td>
<td>Minimal # of staff to maintain reduced operations</td>
<td>Non-routine</td>
<td>YES</td>
<td>High</td>
</tr>
<tr>
<td>D</td>
<td>Closed</td>
<td>Stop</td>
<td>Minimal # of staff required to maintain safety and security of facility</td>
<td>Non-routine</td>
<td>YES</td>
<td>Critical</td>
</tr>
</tbody>
</table>
Pandemic “disruption” : hand Sanitizer AND resume clinical prod.

Hand Sanitizer : NIAID/VRC-funded
- 80% alcohol-based
- FDA: facility registration; temporary guidance
- 13 x 75-Liter batches ; single use systems
- Total supply : 2041 bottles
- Supplied local hospitals & NIH (60%), and FNL (40%)

Resumed Production in May!!
- HIV Vaccines (2)
  - Rec glycoprotein trimer
  - Peptide conjugate (3 components)
  - + Proprietary adjuvant
- Influenza universal vaccine
  - Nanoparticle (5 components)

VCMP: multi-product, GMP facility
- Drug substance : multi-product manufacture - microbial and mammalian
Enterprise-wide “return to the workplace” website resource

COVID-19 Return to the Workplace

COVID Safety: Prepare for a “New Normal”

Our Mission Is the Same, But We’ll Be Doing Things Differently

NIH COVID Guidance for Employees
Communication Center: COVID Messages
Hand Sanitizer Request Form
Order from the Supply Warehouse
Self-Checker
Prevention
DIY Face Coverings
Steps to Disinfect
EPA Disinfectants
Basic science informs assay and vaccine development

CONVENTIONAL
- Viral vector e.g. adenovirus vaccine
- Nucleic acid e.g. pDNA or RNA
- Mammalian cell culture subunit
- Mammalian cell culture nanoparticle

THERAPEUTICS DEVELOPMENT
- Broadly neutralizing and potent mAb(s) expressed in mammalian cell culture
- Evaluate in clinical studies

Cryo-EM structure determined: informs structure-based vaccine design

CONVENTIONAL VITAL VECTORS
- e.g. adenovirus
- Nucleic acid, e.g., pDNA or RNA
- Mammalian cell culture
- Mammalian cell culture nanoparticle

High Quality Protein is the Basis for Next Steps

Isolation of monoclonal antibodies

Assay development

Vaccines
SARS-CoV-2 vaccine landscape: complex “race” to clinic

Novavax Initiates Phase 1/2 Clinical Trial of COVID-19 Vaccine

- First participants enrolled in Phase 1 portion of clinical trial of NVX-CoV2373
- Phase 2 portion to begin promptly following successful Phase 1 results

GATHERSBURG, Md., May 23, 2020 (GLOBE NEWSWIRE) -- Novavax, Inc. (NASDAQ: NVAX), a late-stage biotechnology company developing next-generation vaccines for serious infectious diseases, today announced enrollment of the first participants in a Phase 1/2 clinical trial of its coronavirus vaccine candidate, NVX-CoV2373, a stable, prefusion protein made using its proprietary nanoparticle technology. NVX-CoV2373 includes Novavax’ proprietary Matrix-M™ adjuvant to enhance immune responses and stimulate high levels of neutralizing antibodies. Preliminary immunogenicity and safety results from the Phase 1 portion of the trial are expected in July 2020.

Novavax

AstraZeneca ties up with Emergent Biosolutions to make COVID-19 vaccine in U.S.

AstraZeneca PLC (AZN.L) will tap the production capacity of Emergent BioSolutions Inc (EBS.N) to make AstraZeneca’s COVID-19 vaccine in the United States, boosting British drugmaker’s efforts to bring a vaccine to the market.

The deal comes weeks after the United States pledged up to $1.2 billion to secure 300 million doses of AstraZeneca’s vaccine, which is among the first to move into mid-stage trials.

AstraZeneca

Adenoviral vector

mRNA

Nanoparticle + adjuvant
Unique industry –govt. partnership: messenger RNA technology

- NIAID/VRC – Moderna (mRNA-1273): thru Phase I, in Phase II, planning Ph III…
- Driver: rapid speed to clinic

Gene Synthesis and Platform Technologies

mRNA vaccinology ➤ “disruptive technology”
VCMP: proved capability and capacity to advance protein-based vaccines and therapeutics

Multi-Prong Strategies for COVID-19 protein vaccine

**Conventional:** CHO mammalian cell culture 9-18 months out (!)
- Cell line development in-house or subcontract (e.g. Cellca – Germany):
  - 3-6 month endeavor
  - Goal: high expression, soluble COVID Spike protein with and without furin enzymatic cleavage + variants
- Additional 6-12 months for Process/analytical, then Tech Transfer and clinical production, testing and release for clinic

**Disruptive and/or novel technologies** (timing: yet TBD!)
- **C1 Expression system** (M. thermofilia fungus) protein vaccine
  - Drivers: rapid development / low cost; short mfg. processing times and purported scalability; targeted glycosylation / product quality
  - Goal: COVID-19 Spike Protein-expressing C1 cell lines with and without furin enzymatic cleavage + other variants
- **Spy Tag / Spy Catcher technology** protein antigen nanoparticle vaccine
  - Fuse either spy tag or spy catcher to self-assembling nanoparticles and antigens (e.g. Spike protein)
Conclusions / takeaways

• Continuity plan /actionable framework is paramount to business resilience
  – Includes return to work plan

• Core values are foundational to delivering on commitments
  – Versatility and Compassion

• Science informs vaccine and therapy development
  – Structure-based design

How can you get involved?