JPEO-CBRND

EFFORTS ON THE PLAGUE rF1V VACCINE SINCE 2018

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PROGRAMS EXECUTED ON BEHALF OF THE CHEMICAL AND BIOLOGICAL DEFENSE PROGRAM
AUGMENTING VACCINE CAPABILITIES THROUGH BIOLOGICAL RESPONSE MODIFIER (BRM) CO-ADMINISTRATION

Background
- Pathway to licensure via FDA Animal Rule using pneumonic NHP model
- Recombinant F1-V protein from Y. pestis in aluminum-based adjuvant
- GMP manufactured in single dose vials; Stable at 4°C for >12 years
- Completed a Phase 1 and two Phase 2 clinical trials (CT)
- Safe, well-tolerated, and highly immunogenic in >95% of vaccinated subjects (n = 849)
- Vaccination schedule shown with three doses across six months

WHO Meeting Timeline
- 2018
- 2019
- 2020
- 2021
- 2022
- 2023

Non-clinical Studies
- Confirms the correlate of protection is the serum F1-V ELISA titer
- Confirms rF1V vaccine efficacy at ≥71% against lethal challenge

Contract Award
- DoD awarded contract to Dynavax to improve the rF1V vaccine’s duration and onset of protection

Phase II Begins
- Part 1 of the adaptive CT initiated to evaluate co-administration of CpG 1018®

Phase II Part 2 Begins
- Part 2 of the adaptive CT initiated with a single co-administration method

Where we are Today
- Phase 2 clinical trial fully enrolled
- Phase 2 Part 2 will complete in early 2024
- Condensed 2 dose schedule
- GMP rF1V vaccine in storage and continued stability testing
- Dynavax has available GMP CpG 1018® for single use dosing

Manufacturing
- Completed GMP manufacturing of rF1V vaccine clinical trial material
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Dynavax Technologies
rF1V-1018: A Plague Vaccine For Rapid Response

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Overview: rF1V-1018: A Plague Vaccine For Rapid Response

- CpG 1018® adjuvant (Dynavax Technologies Corporation) is a TLR9 agonist promoting T-helper 1 immune responses used in HEPLISAV-B® (2 doses over 1 month) and 5 COVID-19 vaccines which have received EUA or full approvals worldwide.

- The rF1V antigen has been developed as an investigational plague vaccine by MCS JVAP (US Department of Defense) requiring 3 doses over 6 months.

- In collaboration with the US DoD*, Dynavax is evaluating an improved plague vaccine rF1V-1018 utilizing Dynavax’s proprietary CpG 1018® adjuvant

  - rF1V-1018 is currently in a Phase 2 human trial (N=200)
    - rF1V-1018 (2 doses, 1 month apart) is being compared to the legacy rF1V antigen-only vaccine (3 doses over 6 months)
    - CpG 1018® induces a more rapid and higher response, greater than two-fold higher antibody response after two doses.

- Improved vaccine rF1V-1018 is
  - Being developed to provide protection with 2 doses IM, 1 month apart
  - Intended to enable rapid response
  - Has potential for use in civilian context in endemic areas

*Funding from MCS JVAP Contract W911SR-21-9-0011 is acknowledged
CpG 1018® Adjuvant Enables Higher and More Persistent Antibody Responses in HEPLISAV-B® Adult Hepatitis B Vaccine

- 0, 4-week schedule
- HEPLISAV-B®: 48 weeks after last dose, declined 1.5-fold from peak
- Engerix-B: 28 weeks after last dose, declined 4.6-fold from peak
- HEPLISAV-B® induced superior anti-HBsAg antibodies at all visits
- Similar reactogenicity and safety profile for both vaccines

CLOVER COVID Vaccine Efficacy Study
Subunit Vaccine containing Spike protein + CpG 1018® Adjuvant

SPECTRA: Primary and key secondary efficacy objectives were met

- Primary Endpoint is met: VE against COVID-19 of any severity is 67.2% (LL of 95.72% CI >30%)
- Key Secondary Endpoint 1 is met: VE against moderate-to-severe COVID-19 is 83.7% (LL of 97.86% CI >0%)
- Key Secondary Endpoint 2 is met: VE against severe COVID-19 is 100% (LL of 97.86% CI >0%)

100% of strains were variants. Efficacy against gamma = 92%

Reference: Bravo. Lancet. 22 (2022) 990-1001
rF1V-1018 Plague Vaccine: Phase 2 Clinical Study

Protect with fewer doses in less time

Dynavax Phase 2 - Compares rF1V antigen + CpG 1018® adjuvant (2 doses, 1 month apart) to the historical DoD antigen rF1V-only regimen (3 doses, 6 months) (NCT05506969)

**Part 1** (N=60) completed Jan 2023

- Compare CpG 1018 co-administration vs. mixing at time of use
- Successfully met primary endpoint
- Both CpG 1018 adjuvanted arms demonstrated a greater than two-fold increase in antibodies over the alum adjuvanted control arm after two doses

**Part 2** (N=140) ongoing through 2024

- Study continues with CpG 1018 mixed at time of use
Summary and Next Steps

• A Phase 2 plague vaccine, rF1V-1018 is intended to protect with fewer doses in less time
  • Includes clinically validated antigen rF1V with CpG 1018® a proven adjuvant.

• Preliminary analysis from Phase 2 study shows rF1V-1018 results in a rapid and higher antibody response with 2 doses IM in 1 month.

• NHP challenge studies are underway to generate correlates of protection data that may be used under FDA Animal rule for near term use under EUA and future approvals.

• Furthermore, with its potential for more rapid and higher immune responses, rF1V-1018 may be considered for future clinical studies in endemic settings.
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