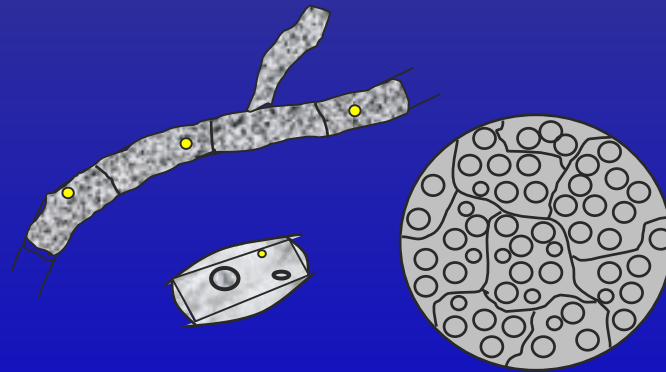


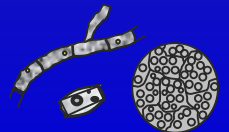
Valley Fever Vaccine Project: where we're headed next.....



Valley Fever Vaccine Project

Goals of Vaccine Project

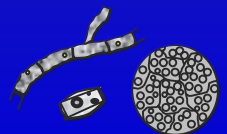
- **Identify a safe and effective acellular vaccine for prevention of coccidioidomycosis**
- **Evaluate the vaccine in humans**
- **Find a commercial partner**



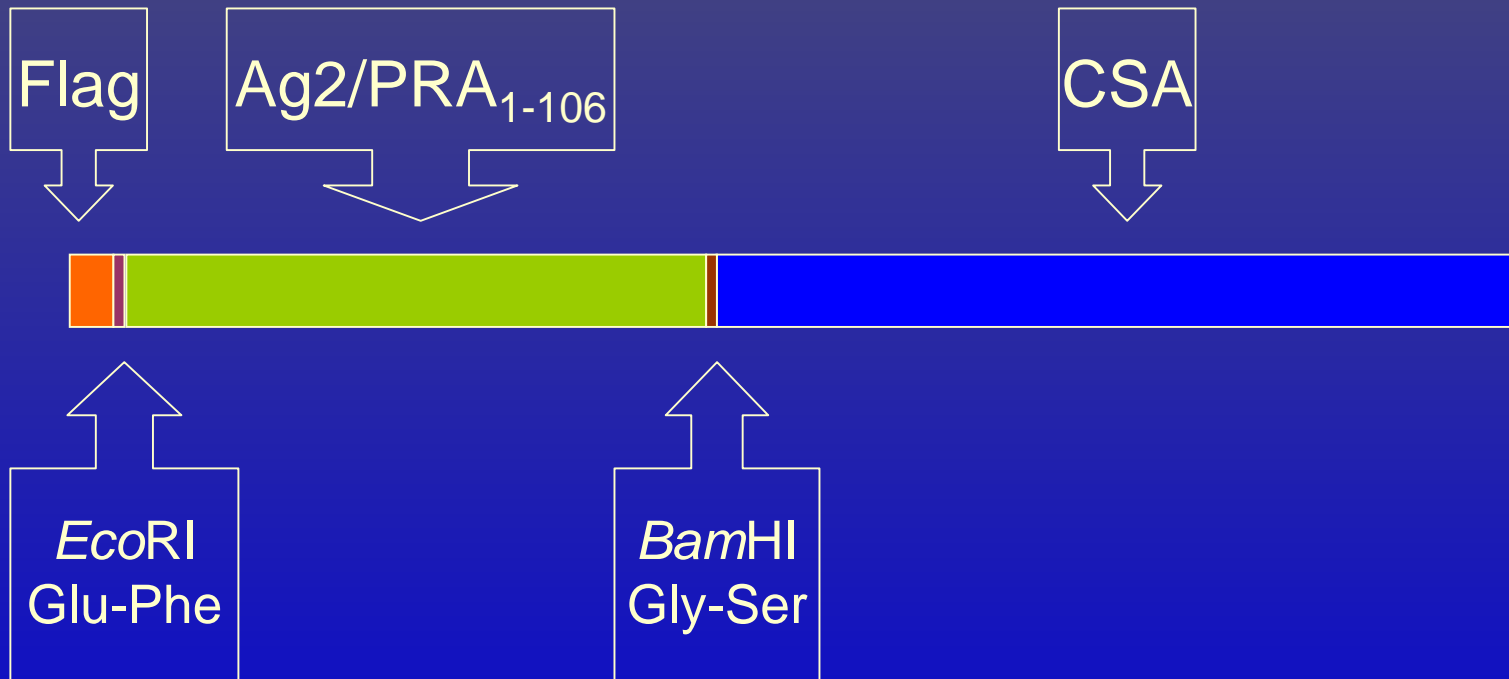
The good news is....

The vaccine is in hand!

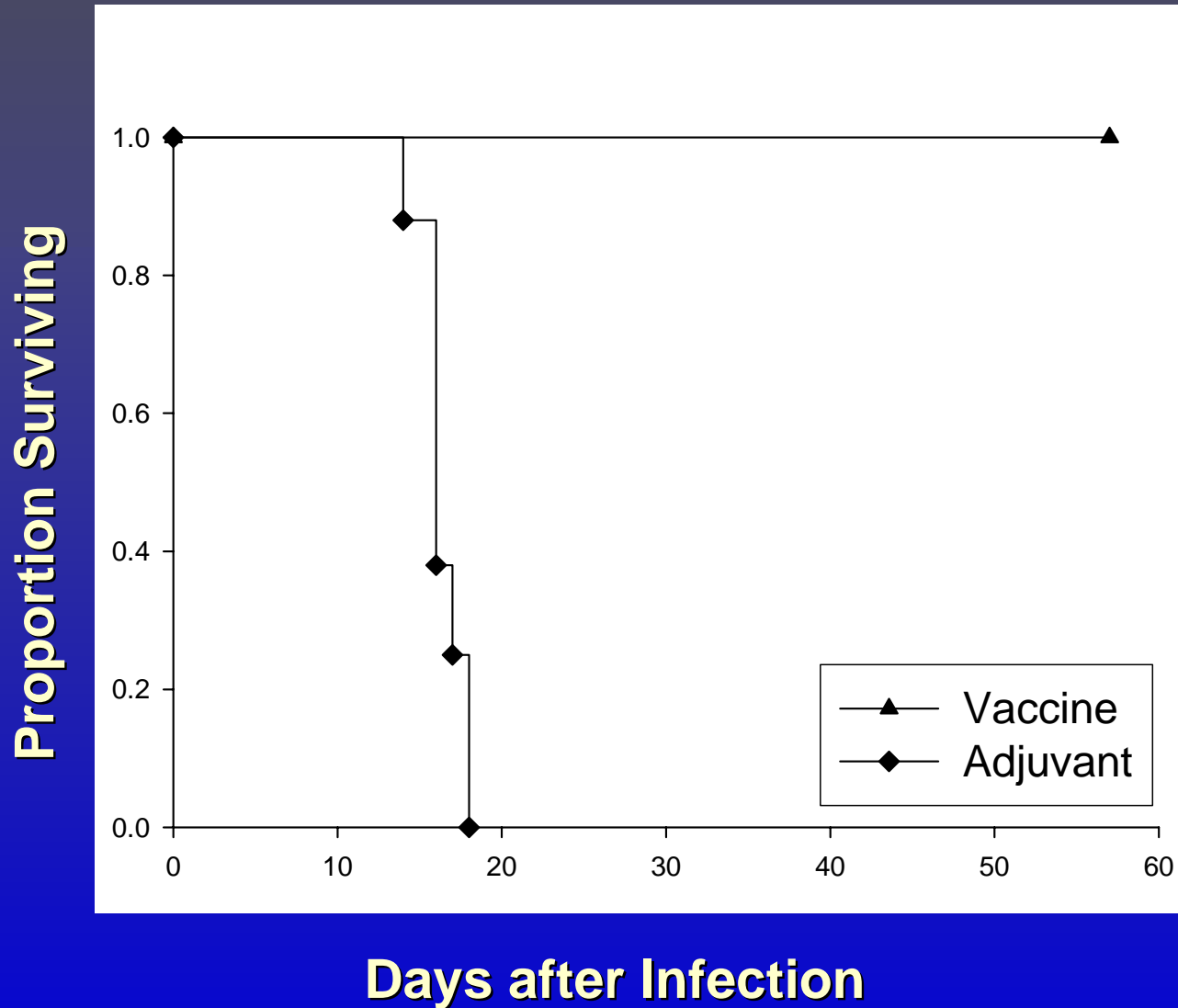
Ag2/PRA106 + CSA chimeric fusion protein



Ag2/PRA106-CSA Chimeric Ag



Protection of Vaccinated Mice

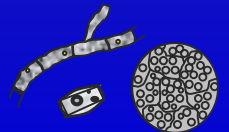


Ag2/PRA106+Csa Fusion Protein

- **Advantages:**
 - 1 manufacturing campaign
 - Simpler formulation & analytical
 - Simpler toxicology testing
 - Simpler, cheaper Phase 1
- **Disdvantages:**
 - No approved fusion protein vaccines on market
 - Harder to interpret negative data or positive tox findings

Roadmap to Phase 1

- **Confirm chimeric protein in primate model**
- **Initiate manufacturing development**
- **Establish analytical methods & formulation**
- **Prepare for pre-IND meeting**
- **Conduct GLP toxicology testing**
- **cGMP manufacturing**
- **File IND**
- **Initiate Phase 1**



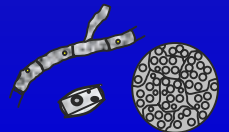
Primate Study of Fusion Protein

3 Phases to study

- **Immunogenicity:**
 - **Doses: 5, 50 $\mu\text{g/ml}$ or adjuvant control**
 - **Given: 0, 1, & 3 months**
 - **Bleed: after each dose for antibodies and IFN-g**

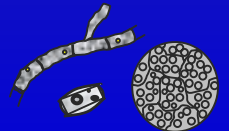
Primate Study of Fusion Protein

- **Safety parameters used to assess**
 - **Draize scores**
 - **Body weight**
 - **Temperature**
 - **Behavior**
 - **CBC, chemistry panel**



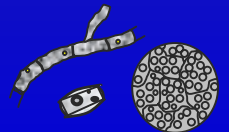
Primate Study of Fusion Protein

- **Challenge:**
 - Infected with 2500 conidia
 - BALF & bleed at intervals
 - Antibody and IFN-g levels
 - Monitor for 90 days: X-rays, CBC, health observations
 - Necropsy
- **Positive results “trigger” pharmaceutical development**

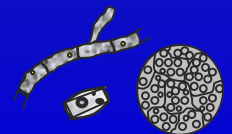
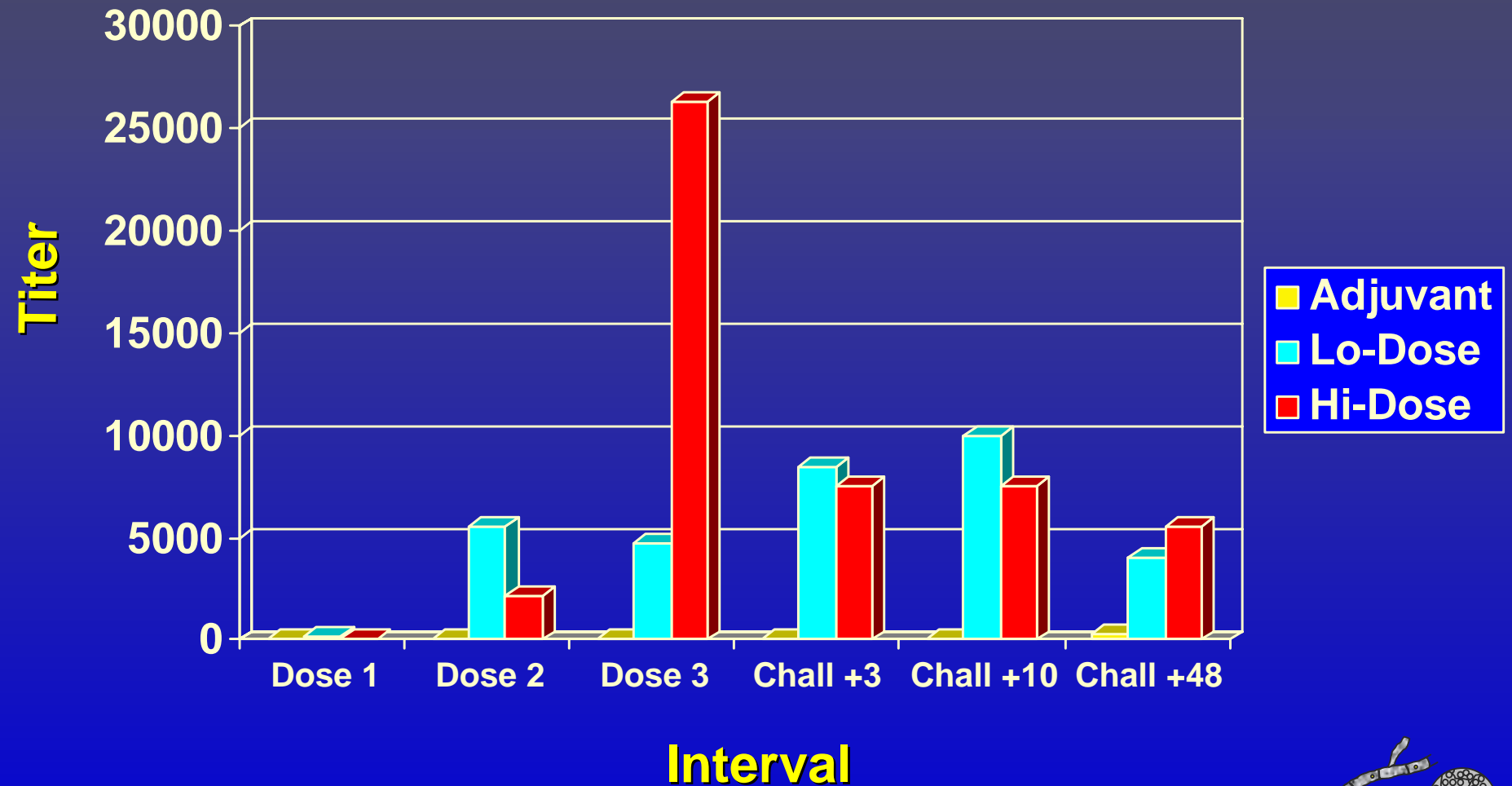


Primate Study of Fusion Protein

- **Current status:**
 - **Animals received 3 vaccine doses**
 - **Doses were well-tolerated**
 - **Vaccinated animals made significant antibody and IFN-g levels**
 - **Animals were infected; all became ill**
 - **Animals necropsied end of July**



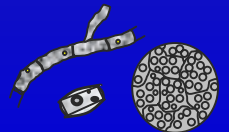
Antibody Titers to Vaccine



IFN- Levels* in Lung

Group	Pre- Infect	Chall. +3	Chall. +7	Chall. +10
Adjuv.	0	0	0	56
Lo-Dose	7	11	370	613
Hi-Dose	286	907	959	1624

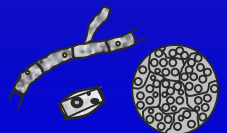
* ng/ml



X-ray Scores*

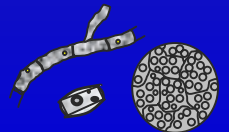
Group	Day 28	Day 56
Adjuvant	3.75	3.5
Lo-Dose	3.5	2.75
Hi-Dose	1.4	1.4

*1= mild signs 9= extreme signs

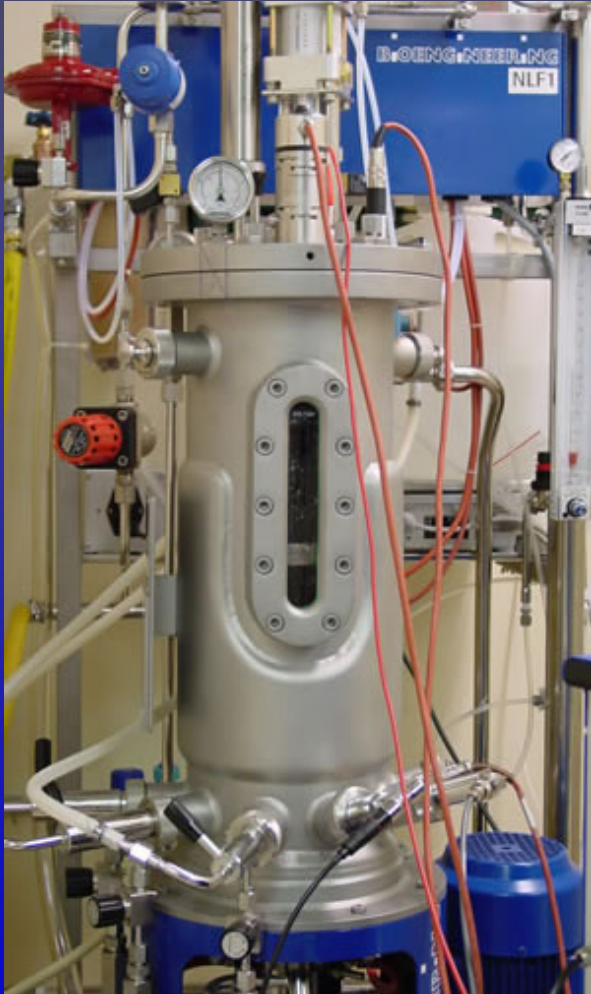


U. Nebraska Biological Process Development Facility

- Selected as manufacturing subcontractor
- Pilot-scale and cGMP manufacturing in same facility
- Focus is early-stage vaccine production
 - Recipient of DoD/NIH funds for BT vaccines
 - Taken 8-9 projects into clinical trials
- VFVP process development now underway



U. Nebraska Biological Process Fermentation Facility



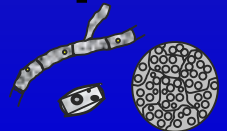
Saccharomyces vs. Pichia?

- *Saccharomyces*

- Our present yeast host, protein already characterized, & all our animal data comes from this strain, but....
- It is a research strain that doesn't grow well

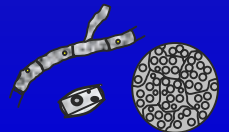
- *Pichia*

- Can be grown to 25X the cell density, but...
- We don't know how the protein will compare in the animal models

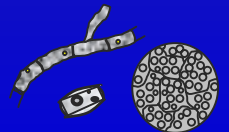
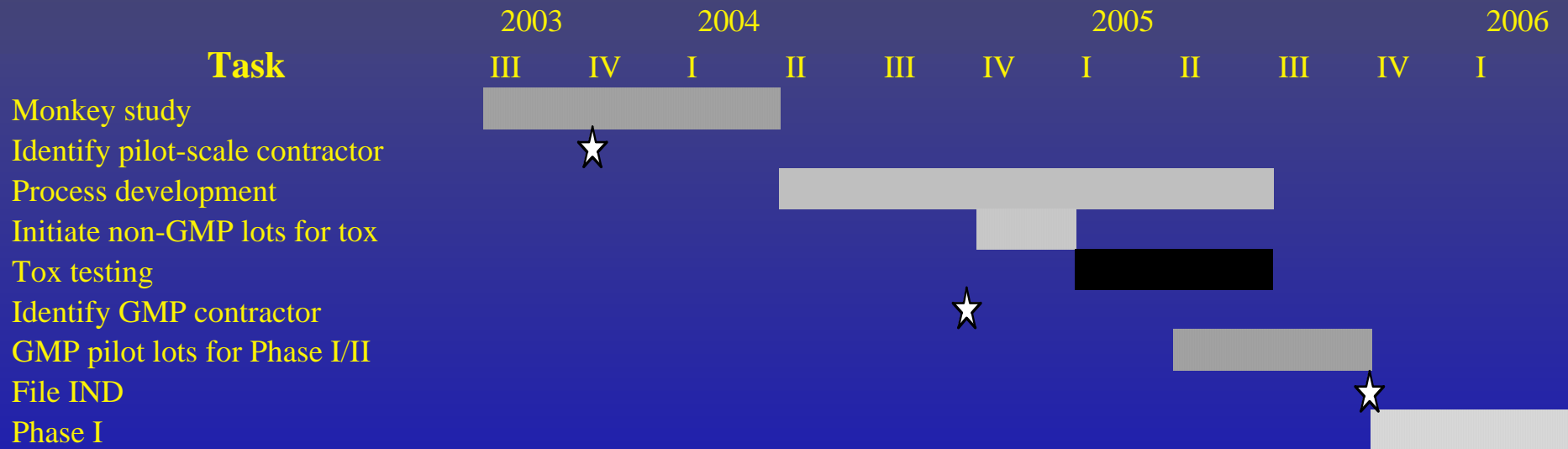


Phase 1 Human Trial

- Perform in normal subjects outside endemic area, age 18-40
- Study 2-3 dose levels vs. adjuvants
 - Dose 0, 1, & 6 months (to be determined)
- Will use facility with vaccine Phase 1 experience

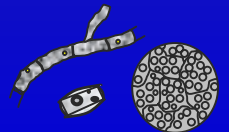


Timelines



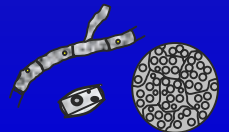
Development Budget*

Activity	05-'06
Pilot Manufacturing	100,000
Formulation	50,000
GMP Manufacturing	1,200,000
Fill/Finish	100,000
Stability/analytical	75,000
Toxicology	55,000
Primate trials	180,000
UCSF	440,000
Regulatory expenses	20,000
Phase 1 trial	400,000
	\$2,620,000



Supporting Organizations

- **CHCF**
- **State of California DHS (Ashburn)**
- **CDC (via Congressman Thomas)**
- **VFVPA & Rotary & VFVF**
- **Kern County**
- **NIAID (genome project)**



we

FIGHT

the

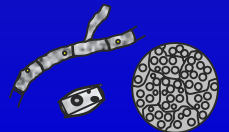
FEVER

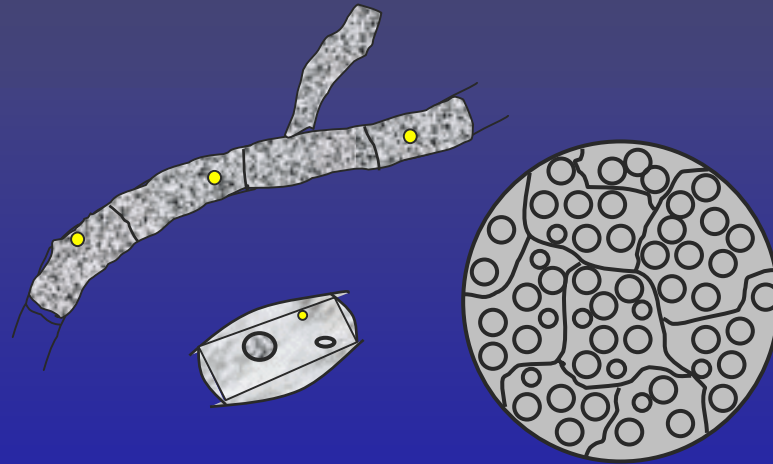
valleyfever.com

**VALLEY FEVER
MORTGAGE FOUNDATION**

Overall Status

- The VFVP has met its research goals
- We have a good, immunogenic vaccine
- We have a plan that takes us to human trials
- We have expectations of success but...
- We need time, effort & continued financial support to reach Phase 1





Valley Fever Vaccine Project