NIAID's Current Development Efforts and Resources for Product Development Targeting Valley Fever

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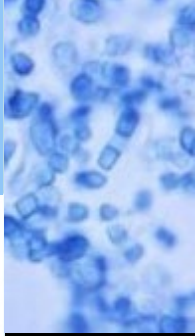
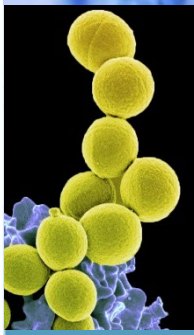
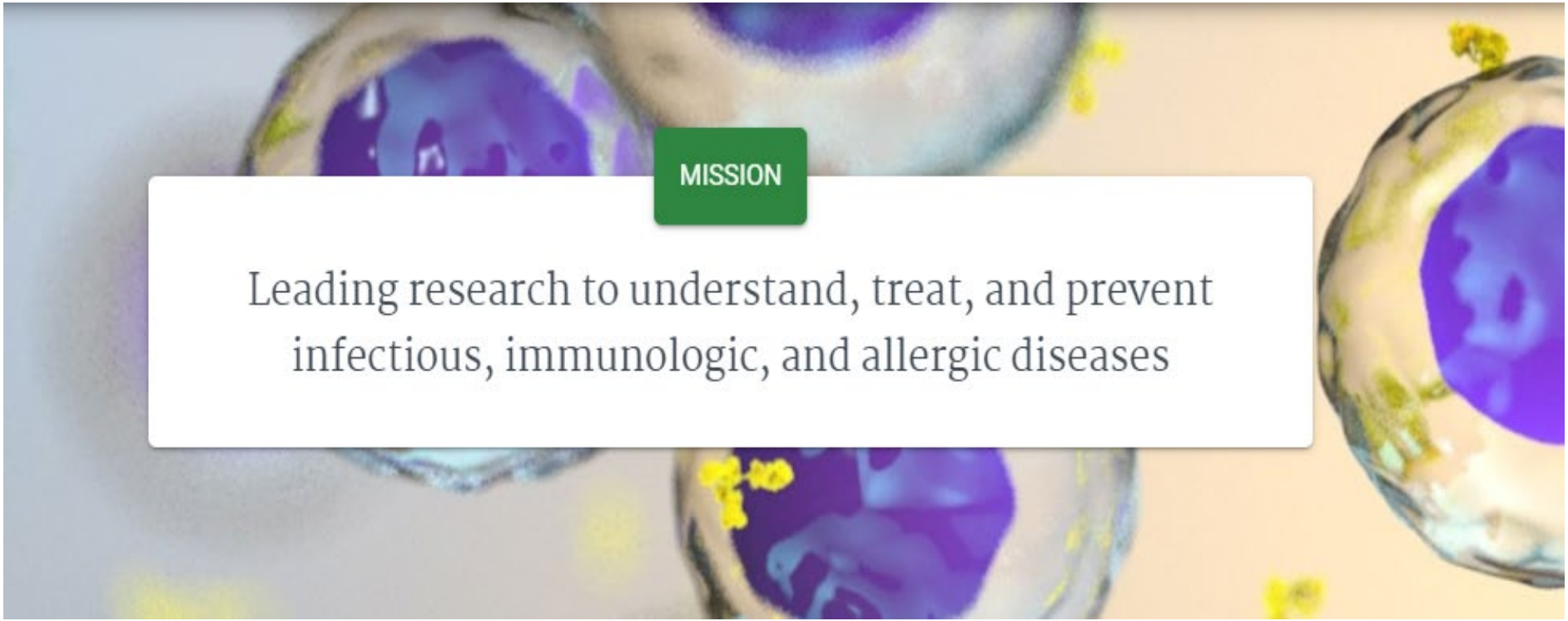




NIAID

Mission of the National Institute of Allergy and Infectious Diseases (NIAID)



DMID Mechanisms to Support Product Development and Reduce Product Development Risk

NIAID support for Coccidioidomycosis in 2019: ~$10 Million

Monoclonal antibodies
Phage Vaccines Diagnostics
Non-traditional antibiotics
Small molecules
Peptides Host-targeted therapies

Investigator-Initiated Grants & Contracts

Funding opportunities for grants and contracts to support basic, translational, and clinical research

Preclinical Services

Ph1 & IDCRC

Free services available to product developers

DMID supports therapeutic and diagnostic development for Valley Fever

- Grants and preclinical services have been utilized by product developers to support programs targeting Coccidioidomycosis treatment and diagnosis
  - Fosmanogepix, Amplyx Pharmaceuticals Inc (grants)
  - VT-1598, Mycovia Inc (grants and preclinical services*)
  - Nikkomycin Z, Valley Fever Solutions Inc (grants and preclinical services*)
  - Olorofim, F2G Inc (preclinical services*)
  - PAs (R01/R21) targeting endemic fungal pathogens/fungal diagnostics
    - 1 R01 & 4 R21s awarded in Fiscal Year 2020
  - SBIR contract topic: Fungal diagnostics for endemic pathogens
    - 4 awards in Fiscal Year 2020, 2 focused on coccidioidomycosis

**to support confidentiality, receipt of preclinical services is only noted if the study is published*

DMID supports vaccine research and development for Valley Fever

- Grants and preclinical services have been utilized by vaccine developers to support programs targeting Coccidioidomycosis.
  - Live attenuated strain (Δcps1), University of Arizona
  - Recombinant chimeric polypeptide antigen (rCPA2), University of Texas San Antonio

Valley Fever update—Community Engagement

2019 NIAID Workshop: Vaccine Strategies for Endemic Fungal Pathogens

- Purpose: bring community together, discuss latest discoveries and determine actionable steps to advance fungal vaccines
- Over 100 people attended by webcast or in person
- **Outcomes:**
  - Expanded the field of investigators
  - Initiated new scientific collaborations
  - Informed NIAID of scientific gaps leading to program announcements and opportunities
    - Identifying new antigens/vaccine candidates
    - Understanding correlates of protection and biomarkers
    - Strengthening preclinical and clinical testing
    - Overcoming manufacturing hurdles, including identifying optimal adjuvants

Valley Fever update — DMID Council-approved targeted initiative

Coccidioidomycosis Collaborative Research Centers - proposed FY22 initiative

- Objective: To establish highly collaborative, multidisciplinary, research teams to conduct translational and clinical research for the improved diagnosis, treatment, and prevention of coccidioidomycosis (Valley fever).
- It is expected that the multidisciplinary centers will leverage unique research resources and patient populations from endemic regions to advance the field.

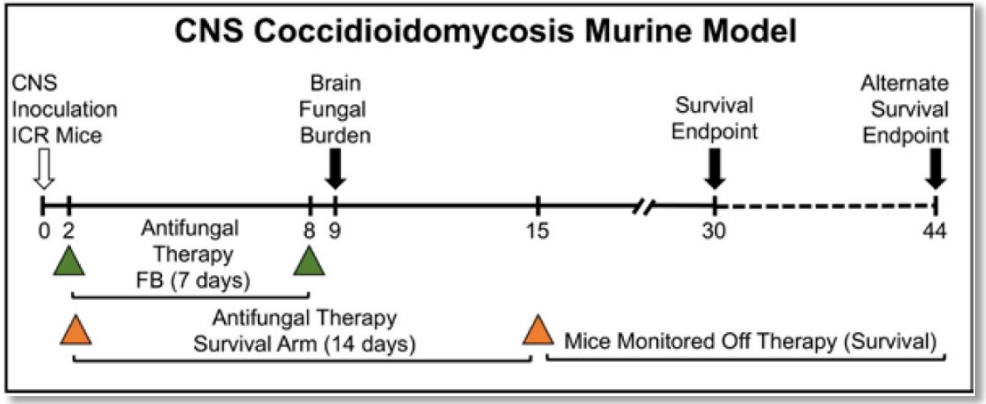
DMID Preclinical Services (PCS) – Suite of contracts supporting anti-infective product development

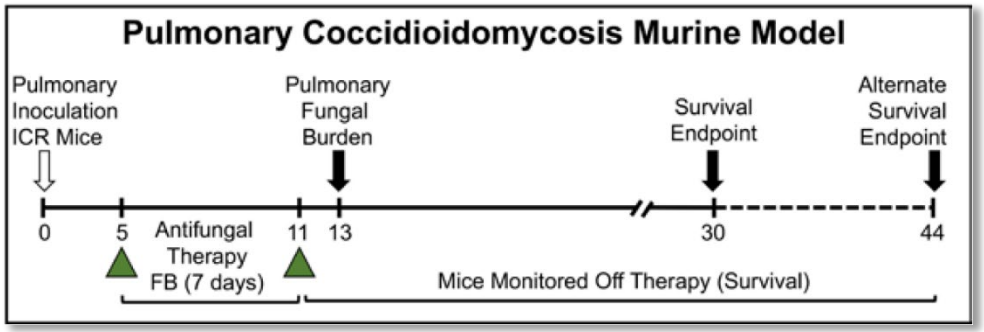
- Gap-filling services, not intended to take a product to licensure
- Lower the risk and advance promising discoveries along product development pathway

Eligibility

- Innovators from academia, non-profit organizations, industry, and government
- Domestic or foreign institutions
- Do not need to have NIH funding
- Simplified Request Process – available year-round

PCS – Testing in Coccidioidomycosis infection models requires models provide supportive data to antifungal drug development programs





Since 2015, DMID's preclinical services has provided:

- MIC testing against Coccidioides species for 25 compounds from 18 institutions
- Testing drug efficacy in Coccidioidomycosis infection models to 5 institutions

Contractors: Thomas Patterson and Nathan Wiederhold, University of Texas Health Science Center, San Antonio

PCS – Preclinical studies help support antifungal drug programs at multiple stages of development

- Medicinal chemistry and process chemistry/scaleup (incl GMP)
- *In vitro* and *in vivo* preclinical toxicology and pharmacokinetics (incl IND-enabling GLP studies)
- Rapid ADMET & PK screening for optimization of lead series
- Preclinical development, planning and evaluation, IND documentation
- Vaccine Testing
- Vaccine Manufacturing

Contractors to date that have performed for antifungal programs: University of Texas Health Science Center, San Antonio; SRI International; Eurofins Panlabs, Inc.; RTI International

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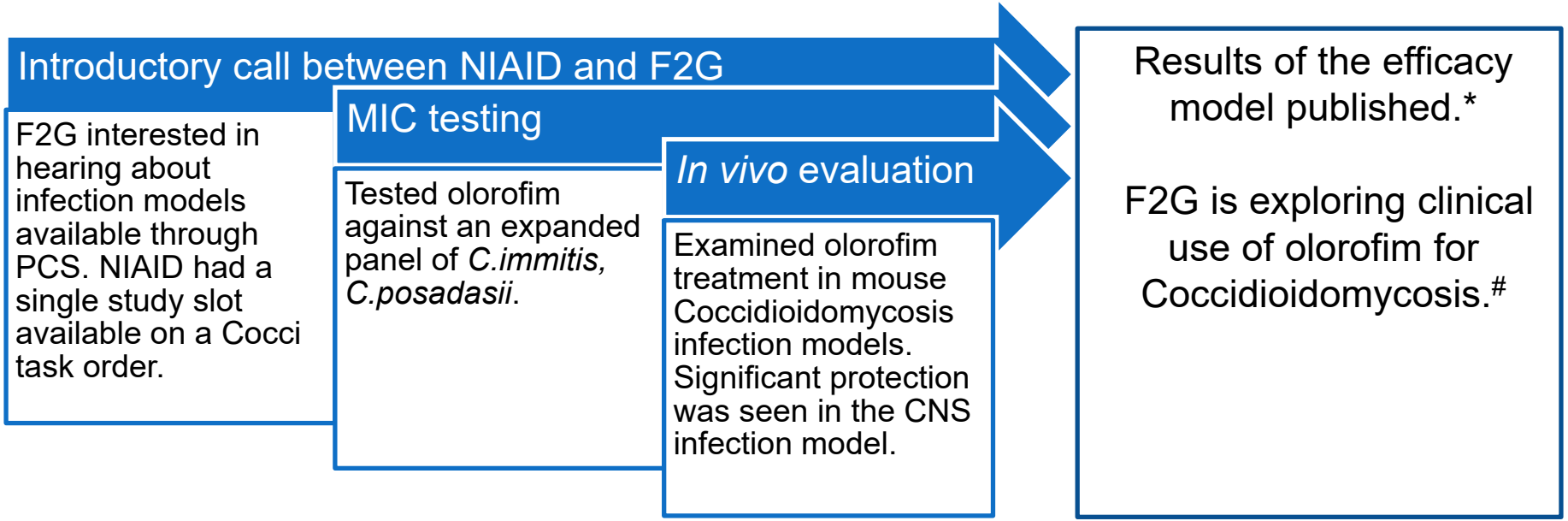
Prior to an in vivo efficacy study:

- ☑ Sufficient compound quantity
- ☑ MIC testing against model strain
- ☑ Analyze pharmacokinetics of the drug in brain and plasma
- ☑ Verify that drug administration is tolerated in ICR mice for planned dosing schedule and duration

Contractors to date that have performed for antifungal programs: University of Texas Health Science Center, San Antonio; SRI International; Eurofins Panlabs, Inc.; RTI International

Please reach out to us!

Tell us about your antifungal programs, and let us know where you need help.



** Wiederhold NP, Najvar LK, Jaramillo R, Olivo M, Birch M, Law D, Rex JH, Catano G, Patterson TF. 2018. The Orotomide Olorofim is Efficacious in an Experimental Model of Central Nervous System Coccidioidomycosis. Antimicrob Agents Chemother.*

 # Harvey 2020 ECCMID, Abstract #3203:Successful use of the novel antifungal olorofim in the treatment of disseminated coccidoiodomycosis

DMID Valley Fever Clinical Services – Ph1 Trial Units

- Contracts provide services, not direct funding, for all aspects of the clinical trial
- NIAID sponsors the trial and holds the IND

ClinicalTrials.gov NCT04208321

Status	Study Title	Conditions	Interventions	Locations
Recruiting	Safety and Pharmacokinetics of **VT-1598**	• Coccidioidomycosis	• Other: Placebo • Drug: **VT-1598**	• ICON Early Phase Services Clinical Research Unit San Antonio, Texas, United States

- VT-1598 is a novel antifungal compound with activity vs. Coccidioides spp.
- Phase 1 single ascending dose study in 48 healthy adults 18 - 45 years of age
- Primary Objectives:
- 1) To determine the safety of single-ascending oral doses of VT-1598 in healthy adult subjects in a fasted state
- 2) To determine the safety of single oral dose of VT-1598 in healthy adult subjects in a fed state.

DMID Valley Fever Clinical Studies – SAnds-PPC

ClinicalTrials.gov NCT03908632

Status	Study Title	Conditions
Recruiting	An Observational Study to Assess the Prevalence and Outcomes of Primary Pulmonary Coccidioidomycosis in Persons Aged > / = 14 Years Presenting With Community Acquired Pneumonia (CAP) in Endemic Areas (SAnds-PPC)	• Coccidioidomycosis • Pneumonia

- Observational study of up to 1,000 individuals aged ≥14 years
- Primary Objective: To assess the prevalence of primary pulmonary coccidioidomycosis (PPC) in subjects with CAP in coccidioidomycosis endemic areas.
- STEP 1: Estimate the prevalence of PPC among individuals presenting with CAP within 28 days of symptom onset
- STEP 2: Follow individuals diagnosed with PPC for up to 24 months
  - Clinical course
  - Predictors of clinical course
  - Response to prescribed antifungal therapy vs. no antifungal therapy

Interested in hearing more about how NIAID can help support your antifungal drug program? Please reach out to us!

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Fungal Clinical Trial Support
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DMID's Bacteriology and Mycology Branch