OUTLINE

- Introductions
- Drug Development
- Cholera
- Cryptosporidium
- Soil-Transmitted Helminths
- Asian Liver Flukes
- Malaria
- Visceral Leishmaniasis
- Future Opportunities
HOW MANY OF YOU...

- are seniors?
- are going to med school?
- are going to grad school?
- have worked in a research lab?
- have visited/lived in a developing country?
ABOUT ME

- Berkeley
- BS, UC San Diego/Salk Institute
- PhD, U of Washington
- Exelixis, Inc (10 years)
- OneWorld Health/PATH (5 years)
THE PROBLEM

- ~1,400 new drugs approved (1975-1999): only 16 (1.1%) for NTDs
- 6 million child deaths: >98% in developing countries
- 32 B-747s crashing every day
PATH DRUG DEVELOPMENT PROGRAM
(FORMERLY INSTITUTE FOR ONE WORLD HEALTH)

- Safe, effective and affordable new medicines for people with infectious diseases in low-resource settings
- iOWH founded in 2001: First US non-profit pharmaceutical company
- In 2012, iOWH became the drug development unit of PATH
PATH’s global reach

Work in more than 70 countries. Offices in 22. 118 million people served last year.

- 6.7 billion vaccinations delivered safely with SoloShot™, the first autodisable syringe
- 100 million children protected from Japanese encephalitis
- 86 million HIV rapid diagnostic tests purchased
- 24.5 million Indians reached with education on safe pregnancy
Core expertise across five platforms
Innovation happens here

Vaccines
Drugs
Diagnostics
Devices
System and service innovations
PRODUCT DEVELOPMENT PARTNERSHIPS

Drugs for enteric diseases
Malaria vaccine RTS,S
Meningitis vaccine MenAfriVac
Japanese encephalitis vaccine
Diagnostics for NTDs

Malaria treatment
Malaria chemoprophylaxis

Visceral leishmaniasis
Sleeping sickness, Chagas
Lymphatic filariasis

Drugs for tuberculosis
Vaccines for tuberculosis

PDPs accounted for 56% of approvals for neglected diseases from 2009-2013
Cohen et al., 2014 Clin Ther
DRUG DEVELOPMENT FUNDAMENTALS

Costs ($100M-$1B)

Attrition Risk

Basic Science Research (target and lead development)
Pre-Clinical Testing
Clinical Trials
Gov’t Approval

1 to 3 years (avg. 18 months)
2 to 10 years (avg. 5 years)
2 months to 7 years (avg. 24 months)
ROUTES TO NEW DRUGS FOR NEGLECTED DISEASES

- **Start from scratch**
- **Hit from academic lab**
- **Repurposing:**
  - Old drugs
  - Abandoned drugs
  - Veterinary drugs
- **New formulations**
- **New combinations**

**Flowchart:**
1. Basic Science Research (target and lead development)
2. Pre-Clinical Testing
3. Clinical Trials
4. Gov’t Approval

**Timeline:**
- 1 to 3 years (avg. 18 months)
- 2 to 10 years (avg. 5 years)
- 2 months to 7 years (avg. 24 months)
CHOLERA

- Acute, life-threatening diarrhea
- Outbreaks: refugee camps, etc. (e.g. Haiti)
- Seasonal epidemics (e.g. Bangladesh)
- Oral rehydration, antibiotics
CRYPTOSPORIDIIUM

- Acute, life-threatening diarrhea
- Potential veterinary indication

Asymptomatic infections:
- Malnutrition
- Growth stunting
- Cognitive deficits
- Oral vaccine failure
SOIL-TRANSMITTED HELMINTHS

- >1 billion infected
- Growth stunting, anemia
- Mass drug administration
-威胁 by drug resistance

Ascaris  Hookworm  Whipworm
ASIAN LIVER FLUKES

- 25 million infected in East/Southeast Asia
- Associated with raw river fish consumption
- Incurable cholangiocarcinoma
MALARIA

Agricultural method

Cultivation

Extraction

Artemisinin

Artether
Artesunate
Artemether
Artemisia
DihydroArtemisinin

Lead time from seed to ACT is ~15 months

Semi-synthetic method

Fermentation

Photo-Chemistry

Artemisinin

Artemisinic Acid

Dihydro-artemisinic Acid

Lead time from lab to ACT is ~3 months

Artemisinin Derivatives

Companion Drug

Lumefantrine (A-L)
Amodiaquine (AS-AQ)
Mefloquine (AS-MQ)
SP (AS-SP)
Piperaquine

...
SEMI-SYNTHETIC ARTEMISININ FOR MALARIA

R & D
- Discovery of the metabolic pathway and identification of genes from the wormwood plant required to make artemisinic acid
- Construct biosynthetic artemisinic acid pathway and clone into microbial host
- Optimize artemisinic acid production

MANUFACTURING
- Optimize microbial strain
- Develop scalable processes for manufacture and purification of artemisin
- Demonstrate comparability of plant derived versus semi-synthetic artemisin

SANOFI
- Fermentation process development
- Chemistry process development
- Develop scalable industrial manufacturing process
- Production and commercialization

AMYRIS
- Project and alliance management
- Enable adoption of semi-synthetic artemisin into supply chain
- Apply WHO sanctioned global health goals to malaria ACTs

2005 2006 2007 2008 2009 2010 2011 2012 2013

OneWorld Health, a drug development affiliate of PATH
VISCERAL LEISHMANIASIS

- 90% fatal if untreated

Paromomycin intramuscular injection:
- Repurposed aminoglycoside antibiotic
- Approved in India, Bangladesh, Nepal
- WHO Essential Medicines List
FUTURE OPPORTUNITIES

- Networking
- Internships
- Low-resource setting experience
- Traditional biotech/pharmaceutical drug development
THANK YOU!