

***Changing the Landscape:***  
**Public-Private Partnerships and the Fight Against  
Neglected Diseases**

**October 2007**

**PPP Analysis - RW**

## The Origins...

*"If Canada is to have a sustained impact on global development issues, it will not be because of the size of our economy or the strength of our army – it will be because of the power of our ideas and the impact of our innovation. My belief in the importance of innovation – and the incredible potential of Canadian innovators – underscores my entire Global Youth Fellowship application. As a result, I intend to use my Fellowship to explore how the research of some of Canada's leading scientists can be more efficiently and effectively harnessed to accelerate the discovery, development and delivery of the drugs needed to combat neglected global health pandemics."*

...from my original Global Youth Fellowship submission - May 2006

# The Key Questions I'm Trying to Answer

How are public-private partnerships fundamentally re-shaping the neglected disease landscape - and where will they go next?

What is Canada's contribution to global health - and what kind of leadership has clustered around the University of Toronto?

What role can MaRS play in helping Canadian scientists and researchers address this pressing challenge?

*This research summary is about answering my **first** question...*

# Outline

- **Introduction**
  - Neglected Disease Overview
    - o Chagas
    - o Visceral Leishmaniasis
    - o Malaria
    - o Tuberculosis
    - o The Worst of the Rest
  - The Truth c. 2000
  - How Drugs are Developed
  - The Sea Change: The Gates Foundation etc.
- The Last 5 Years
  - Case Studies
    - o Drugs for Neglected Diseases Initiative
    - o The Institute for One World Health
    - o Medicines for Malaria Vaccine
    - o TB Alliance
  - Big Questions
  - Recommendations
  - Conclusions

# The Immense Impact of “Neglected Diseases”

- “Neglected diseases” still kill more than 3 million people every year – with children and pregnant women the most vulnerable populations - and cost the equivalent of almost 100 million years of lost life.
- By their very definition, neglected disease like TB and Malaria - and more than a dozen other afflictions - have historically failed to attract significant investment. As a result, the poorest and most disadvantaged citizens are excluded from the potentially transformative impact of modern pharmaceutical therapies - further compounding the devastating impact of these diseases.
- Because they affect the citizens of developing countries, neglected diseases also exacerbate economic insecurity, environmental degradation and civil conflict. They are a blight on the global community.

## A New Cause for Hope...

- Since the late 1990s, however, the emergence of a critical mass of public-private partnerships (PPPs) has revolutionized the discovery, development and deployment of pharmaceuticals designed to mitigate these diseases.
- It was this discovery that ultimately shaped and focused my Fellowship, that excited and energized my research, and that left me exposed to a new generation of innovators determined to help some of the world's poorest and most marginalized citizens. In other words, it was this discovery that pulled me through the past 16 months – and that continually reminded me of just how privileged I was to be able to spend such a sustained period of time working on such important issues.

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# Just what is a “Neglected Disease”?

*Interestingly enough, there is no single universally accepted definition of “neglected diseases.” That said, a general and widely-accepted consensus has emerged:*

- Diseases are “neglected” if the people suffering their impact are generally too few or too poor to create a normal, sustainable market for the discovery, development and delivery of innovative new pharmaceutical products.
- Although a small market for some of these disease often exists in developed countries, it is insufficient to attract any kind of sustained research and development investment.
- Some remedies to neglected diseases DO exist, but treatment methods tend to be decades out of date - and their relevance and efficacy increasingly questionable.
- International attention tends to focus on tuberculosis and malaria - but there are at last 12-15 other diseases that fall into this category.

**“Most neglected”** diseases are those where the patients are so poor that virtually no market exists - and therefore no commercial interest.

- **Examples include human African trypanosomiasis, Buruli ulcer, Chagas disease and Leishmaniasis**

# The Strange Case of HIV/AIDS

- By any standard measure of research \$ invested, HIV/AIDS is NOT a neglected disease - and yet many of the organizations working in the neglected disease space also focus on the disease.

## **WHY?**

- HIV/AIDS is a disease of the immune system. HIV/AIDS is itself rarely fatal; instead, it weakens the body's ability to withstand infection - and therefore leaves it susceptible to secondary or "follow-on" diseases like TB or malaria.
- As a result, many research and advocacy organizations focusing on population health and wellness issues and health system development will group the three diseases together, with the most notable example likely the Global Business Coalition on HIV/AIDS, TB and Malaria.
- Another reason for this focus is the stigma that still surrounds HIV/AIDS in many developing countries, which can leave patients underserved by local health authorities.
  - Exhibit A is South Africa during the late 1990s and early 2000s, where the Minister of Health achieved international notoriety by recommending garlic as her preferred therapeutic.

**For the purpose of this project, HIV/AIDS is not included as a neglected disease.**

# "Neglected Diseases" - The Big 4

*Although more than 15 diseases qualify as "neglected" - depending on the definition used - 4 are especially pervasive and impactful:*

## **Chagas**

- Chagas is the third most impactful parasitic disease in the world - after malaria and schistosomiasis.
- Prevalent across Latin America, it causes 50,000 deaths a year.
- With 120 million people at risk, Chagas affects 16-18 million people in 21 countries.

## **Visceral Leishmaniasis**

- 500,000 new infections of VL occur every year; without treatment, death is virtually certain.
- VL is endemic in 65 countries, with an at-risk population is estimated to exceed 200 million people.

## **Malaria**

- Malaria is a life-threatening disease transmitted by mosquitoes that have been infected by *Plasmodium* parasites
- It kills between 1-3 million people every year, with annual infections approaching 600 million.
- Malaria kills a child in Africa every 30s and Malaria costs the countries of Africa more than \$14B in annual GDP.

## **Tuberculosis**

- TB kills someone every 20 seconds - about 4,400 people every day, or approximately 1.6 million in 2005 alone.
- TB is second only to HIV as the leading infectious killer of adults worldwide and it accounts for more deaths among women than all other causes of maternal mortality combined.

# Chagas

# Chagas

## *Characteristics*

- Chagas disease - also known as American trypanosomiasis - is a parasitic disease that afflicts millions of impoverished people across Central and South America.
- There are two phases:
  - o The **acute phase** lasts for no more than the first few weeks or months after infection and is characterized by mild symptoms - fatigue, muscle aches - easily confused with other ailments. Any symptoms that develop during this period will fade away in their own - but the infection will persist. During the acute phase, young children can occasionally die from severe inflammation/infection of the heart muscle (myocarditis) or the brain (meningoencephalitis).
  - o During the **chronic phase**, the infection can remain silent for decades. When symptoms do emerge however - in 30% of those infected - they can include cardiac complications such as an enlarged heart (cardiomyopathy), heart failure, altered heart rate or rhythm, and cardiac arrest - leading to sudden death and/or intestinal complications such as an enlarged esophagus (megaesophagus) or colon.

# Chagas

## *Transmission*

- Chagas is transmitted by insect vectors called *triatomine* bugs - blood-suckers that pass the *T. cruzi* parasites in their feces.
- The bugs are nocturnal, and emerge from their homes in mud, palm or thatch houses in the evening.
- The bugs tend to feed on the people's faces, which makes it easy for the parasite to enter the bloodstream through breaks in the skin or the mucous membranes.
- People also can become infected by eating uncooked food contaminated with feces from infected bugs, through organ transplantation or blood transfusion, or from a mother to her child *in utero*.
- Interestingly, **chagas disease is not transmitted from person-to-person like a cold or the flu** or through casual contact - unlike TB for example.

# Chagas

## *Distribution & Impact*

- Chagas is endemic in 21 countries across Central and South America
- 16-18 million people suffer from chagas; with another 100 million at considerable risk of infection.
- it is estimated to cause 50,000 deaths a year - and the loss of 3 million disability-adjusted years.
- Recent research suggests that chagas is **the leading parasitic disease in Latin America** - and the third most impactful globally (after malaria and schistosomiasis).
- Originally a rural disease, chagas is now found in major metropolitan area due to migration patterns.
- In isolated instances, **chagas has actually been found in the United States, making it one of the few neglected diseases to penetrate North America.**

# Chagas

## *Current Treatments*

- There are only two drugs currently available to treat chagas:
  - **Nifurtimox** - given in daily doses for 60-90 days.
  - **Benznidazole** - given in daily doses for 30-60 days.
- Neither medication is especially effective for chronic patients.
- Chagas is also difficult to diagnose - and therefore treat - given the vagueness of symptoms during the acute phase, as well as the long latency period for some patients.

# **Visceral Leishmaniasis**

# Visceral Leishmaniasis (VL)

## *Characteristics*

- Also known as *kala-azar*, VL is a generally fatal infection caused by various species of *Leishmania* parasites .
- VL is the most severe form of leishmaniasis - without treatment, death is virtually certain.
- Symptoms include:
  - Drastic weight loss
  - Chronic but irregular fever
  - Anemia (weakness caused by insufficient iron in the blood)
  - Enlargement of the spleen
  - Enlargement of the liver
- Over time, the leishmania parasites infect the bone marrow, which leads to a weakened immune system and an increased susceptibility to follow-on infection and disease .
- Co-infection with HIV/AIDS has become particularly common.

# Visceral Leishmaniasis (VL)

## *Transmission*

- The *leishmania* parasites enter the body of through the bite of any of one 30 species of sandfly.
- The sandflys become carriers by taking a blood meal from a so-called "reservoir host".
- Hosts can include humans and both wild and domesticated animals (including dogs and rats).
- Most leishmanias are transmitted from animal *TO* human
- As a result, VL is most likely to strike people living in poor, rural areas and lacking access to a basic health system.
- VL also also frequently unrecognized and therefore untreated - similar to chagas.

# Visceral Leishmaniasis (VL)

## *Distribution & Impact*

- VL is endemic in 65 countries, most in Asia, South America and Sub-Saharan Africa.
- The at-risk population is estimated to exceed 200 million people.
- 500,000 new infections occur every year - the vast majority (>90%) concentrated in 5 countries:
  - o Bangladesh
  - o India
  - o Nepal
  - o Brazil
  - o The Sudan

# Visceral Leishmaniasis (VL)

## *Current Treatments*

- **Antimonials:** a 28-day intravenous- or intramuscular-injection regime
  - o Resistance rates of ~60% have been reported in some regions.
  - o Although generally expensive, a generic product (costing \$30) is available.
  - o Significant side effects include nausea, pain, inflammation of the pancreas and damage to the heart muscle (cardiotoxicity).
- **Amphotericin B:** 4-6 week intravenous regime
  - o Expensive, and significant side effects including fever, kidney damage and cardiotoxicity.
- **AmBisome:** 5-day intravenous regimen
  - o Minimal side effects, but the most expensive (US\$300).
- **Miltefosine:** 28-day oral regimen
  - o Also expensive, and carries a risk of significant side effects.

### **BOTTOM LINE:**

Current treatments cost b/w US\$30 and \$300 - and many are either ineffective or toxic

# Malaria

# Malaria

## *Characteristics*

- Malaria is a life-threatening disease transmitted by anopheles mosquitoes that have been infected by *Plasmodium* parasites.
- The main symptom of malaria is utter exhaustion - accompanied by high fever, shaking, sweating and chills.
- By destroying red blood cells, malaria can also lead to anemia
- The disease manifests itself in two different forms:
  - Uncomplicated Malaria - characterized by symptoms very similar to a common flu
  - Severe Malaria - characterized by damage to the body's red blood cells, which in turn block vessels to the brain or impact other vital organs
- The result of severe malaria is often death, while uncomplicated malaria can easily evolve into severe malaria in patients lacking any basic immunity to the disease.
- Even those patients with immunity can become asymptomatic carriers of the disease - that is, they can continue to infect others without becoming infected themselves.

# Malaria

## *Transmission*

- When an infected female *anopheles* mosquito bites a human, the *Plasmodium* parasite enters its new host.
- The parasites move into the body's liver and begins dividing rapidly.
- A new form of the parasite emerges - called *merozoites* - and begins to infect the red blood cells.
- Some merozoites serve as the disease "carrier" - and when another female mosquito bites the infected person, the disease moves into the salivary glands of the mosquito and the whole process begins anew as soon as another person is bitten.
- The time from bite to symptom can take anywhere from 7-30 days (or longer, depending on whether any preventative medication has been taken).
- Although the most malignant forms of malaria manifest their symptoms within 3 months, other strains may lay dormant for up to 3 years.

# Malaria

## *Distribution & Impact*

- Malaria kills between 1-3 million people every year
- Annual infections can approach 600 million, leading to 300 million cases of acute illness
- The majority of victims are children under 5 and pregnant women
  - Children are especially susceptible to death, whereas pregnant women tend to be asymptomatic carriers
- More than 40% of the world's population lives in a region affected by malaria, and the disease is endemic in over 100 countries, most notably sub-Saharan Africa (where 90% of deaths due to the disease occur)
  - 2 staggering statistics: **Malaria kills a child in Africa every 30s** and **Malaria costs the countries of Africa more than \$14B in annual GDP**
- Like virtually all neglected diseases, malaria goes hand-in-hand with poverty: 58% of cases are found in the poorest 20% of humanity

**Malaria is arguably the most prevalent and damaging disease on the planet**

# Malaria

## *Current Treatments*

- Two key challenges complicate the fight against malaria:
  - Although a number of drugs exist that are capable of preventing Plasmodium infection, chronic use of these drugs causes serious side effects
  - Traditional first-line treatments - like chloroquine - are no longer effective due to increasing drug resistance.
  - In fact, the emergence of Plasmodium-resistant strains unaffected by these traditional treatments has seen malaria expand to regions where it had previously been eradicated.
- Scientists have responded with a new therapy called ACT - artemisin combination therapy - that combines artemisin with other antimalarial medications.
- The holy grail in the fight against malaria is a vaccine - but even optimistic analysts believe a vaccine is at least a decade away.
- Although outside the purview of this analysis, it is also important to emphasize the importance of prevention techniques such as bednets and insecticides.

# **Tuberculosis**

# Tuberculosis

## *Characteristics*

- TB is essentially a respiratory disease, with symptoms occurring 2-8 weeks after infection.
- It starts by attacking the body's lungs and damages them from within.
- TB can migrate to the back, the kidneys and other organs
- Initial symptoms include fever, night sweats, a dry cough - that can include coughing up mucus or even blood - loss of appetite and weight loss..
- Over time, pleural disease can occur - a rupture of the diseased area into the cavity between the lung and the abdominal cavity.

# Tuberculosis

## *Transmission*

- TB is caused by the bacillus *Mycobacterium tuberculosis*, which is spread by infected patients through the air - sparked by something as simple as a cough or even speaking.
- The bacterium's unique cell wall - almost a waxy coating composed of mycolic acids - allows it to lay dormant for years.
- This latent transmission danger is compounded by the fact that the human immune system can only restrain or slow the disease - it can't destroy it.
- Although only 10% of carriers will develop active TB, the disease's penetration within affected populations is so deep its impact is pervasive.

# Tuberculosis

## *Distribution & Impact*

- The WHO estimates that more than 2 billion people around the world are infected with TB - 1 out of every 3 people on Earth.
- TB is the leading cause of maternal mortality - and kills more women than all other causes combined.
- After HIV/AIDS, TB is the leading infectious killer of adults worldwide
- The connection with HIV/AIDS is a fatal one:
  - o More than 1/3 of the more than 40 million people living with HIV/AIDS are also infected with TB
  - o Unsurprisingly, TB is the leading killer among people with HIV/AIDS

***The numbers are staggering: In 2005, TB killed 1.6 million people. That's 4400 people every day - or one person in the 20s it took me to finish this sentence.***

# Tuberculosis

## *Current Treatments*

- Current TB drugs tend to be more than 40 years old.
- Treatment lasts 6-9 months - a length of time that virtually ensures many patients will find completing the therapy extremely difficult.
- This kind of inconsistent and erratic treatment leads to drug resistance - which is further complicated by the increasing co-infection rates between TB and HIV/AIDS.
- The two most resistant strains are MDR-TB and XDR-TB - both extremely difficult to treat.
  - o 4% of patients have drug-resistant TB - a number that rises to 15% in certain TB hotspots.
  - o XDR - which was only isolated in 2006 by the Centers for Disease Control - is seen as "virtually untreatable"

# The Worst of the Rest

*After TB, Malaria, VL and Chagas, there are six additional "neglected diseases" that merit mention:*

- **Human African Trypanosomiasis (HAT or sleeping sickness):**
  - o Fatal if left untreated, around 60m people in 36 sub-Saharan African countries are at risk.
  - o HAT reduces many victims to an almost catatonic, zombie-like state.
  - o Most drugs are old, difficult to administer and one – Melarsoprol – contains arsenic and can kill up to one in twenty patients.
- **Dengue:**
  - o Another mosquito-borne illness, more than one-third of the world's population is at risk - a stat made all the more sobering by the fact that no specific treatment exists.
  - o Dengue is nicknamed "breakbone fever" because its symptoms include incredibly painful full-body flu-like symptoms.
  - o It affects 100 countries in Africa, the Americas, SE Asia and the Western Pacific. No specific treatment.

# The Worst of the Rest (cont.)

- **Leprosy:**

- o Records of leprosy date to 600 BC.
- o Although leprosy has been virtually eradicated over the last 20 years - in that time 12m patients have been cured and the disease has been wiped-out in 108 of the 122 countries where it was a threat - in 2002 there were still 650,000 cases reported in India, Brazil, Madagascar, Mozambique, Myanmar and Nepal.
- o Effective drugs have been available for 60 years, but the treatment period is prolonged.

- **Lymphatic filariasis (Elephantiasis):**

- o Like Dengue and Malaria, Elephantiasis is spread by mosquitoes.
- o Its characteristics are massive swelling of the limbs and genital area.
- o 120m people are infected around the world - largely in India and Africa - and 1/3 of patients are seriously incapacitated or disfigured.
- o Both **GlaxoSmithKline** and **Merck** have been involved in donating effective medications.

# The Worst of the Rest (cont.)

- **Onchocerciasis (River Blindness):**

- o River blindness is caused by a parasitic worm that can remain inside the body for up to 15 years.
- o Almost 20 million people in tropical Africa are infected
- o 800,000 have impaired vision impairment and another 270,000 are completely blind.
- o However, a single annual dose of ivermectin (brand name **Mectizan**) can dramatically reduce the likelihood of infection.
- o **Merck** has been donating this drug for free for 20 years.

- **Schistosomiasis (Bilharzia):**

- o A parasite picked up from fresh-water snails, Bilharzia affects over 200m people living across the developing world.
- o The disease damages the bladder and the kidneys, but kills relatively few – around 15,000 every year. That said, children are especially vulnerable.
- o Two effective drugs are available – praziquantel and oxamniquine.

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# A Dire Prognosis

- Only 3% of global funding for drug R&D is dedicated to the diseases of the developing world.
- From 1979-2004, **1393** new chemical compounds entered the global pharmaceutical market. Only **13** drugs - or 1% - were for tropical infectious diseases. (*3 were for TB.*)
- Of the 13, 10 were developed for military or veterinary purposes.

**So in the 25 years to 2004, only 3 drugs were created as specific weapons against neglected diseases.**

# An Appalling Lack of Progress

- Some global health activists would argue that the failure to produce new compounds and medications during this period can be laid at the doorstep of “big pharma”.
- The markets - in other words, the populations infected by these neglected diseases - were simply too poor and too small to merit any significant investment in R&D.
- As a result, policymakers entered the new millennium convinced that the only way to close this R&D gap was to artificially stimulate demand - to offer **per-pill or per-drug subsidies** to major drug companies **OR** to pursue “**compulsory licensing**” and break patents to allow generic companies to produce branded medicines at depressed prices.

# What About Partnerships?

*During this period, one significant partnership emerged that continues to play a significant role in the neglected disease space:*

- The WHO's Special Programme for Research and Training in Tropical Diseases (TDR)
  - TDR is an independent scientific research collaboration driven by the WHO, the World Bank, UNICEF and the UN Development Program (UNDP).
  - As well as its R&D focus, TDR is also involved in building scientific and commercialization capacity in developing countries – a systems-based approach that's a key distinguishing characteristic.
- But TDR was the notable exception.

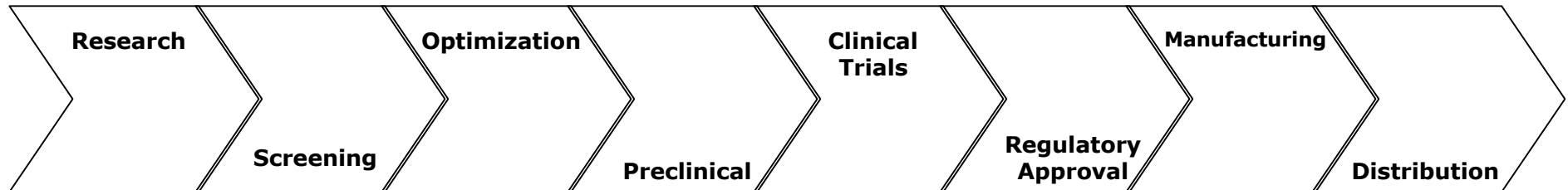
**WHY?** In part because most of the partnership proposals failed to understand the underlying dynamics of the international pharmaceutical market - and this doomed their chances of success.

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# Breaking Down the Drug Development Process

*There are 8 key steps in the development of any pharmaceutical product. At each one, a "go/no go decision must be made - and additional resources committed*



For **EVERY** pharmaceutical produced from "scratch":

**~15-18 Years**

**~\$400 million US**

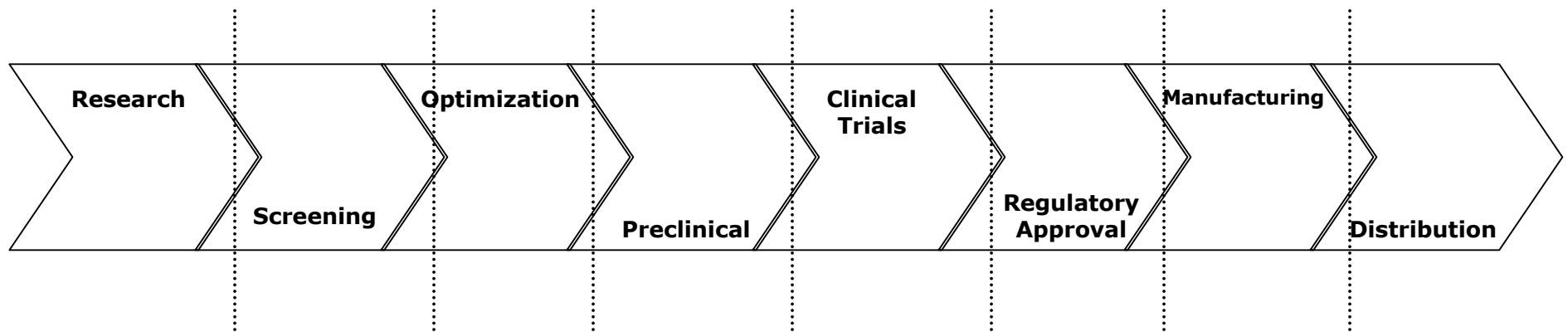
# Breaking Down the Drug Development Process

*There are 8 key steps in the development of any pharmaceutical product:*

- **Research** - Assessing the efficacy of chemical compounds against specific disease markers
- **Screening** - Filtering the most promising leads and protecting the ensuing IP
- **Optimization** - Creating compounds that can be used in clinical trials
- **Preclinical** - Using lab and animal testing to determine safety and effectiveness
- **Clinical Trials** - Measuring impact in human patients; assessing side effects
- **Regulatory Approval** - Submitting clinical trial results to regulatory agencies
- **Manufacturing** - Scaling up production to meet demand from multiple markets
- **Distribution** - Establishing transportation and logistics to move product from manufacturing facilities to wholesalers

# Getting to "Go"

*There are 8 key steps in the development of any pharmaceutical product. At each one, a "Go/No Go" decision must be made - and additional resources committed*



**These "Go/No-Go" decisions are very complicated - and very costly**

# How the Decisions are Made

*Companies select promising drug development leads using a bucket of diverse criteria:*

- **Market size** - How large is the potential market?
- **Competitive landscape** - How many competitors are in the space?
- **Cost of synthesis** - How expensive will it be to turn the relevant compound into a product?
- **Ease of synthesis** - How quickly can you turn the relevant compound into a product?
- **Effectiveness** - How well will the drug work?
- **Toxicity** - What side effects will it cause? How serious are they?

*In the neglected disease space, key additional criteria come into play:*

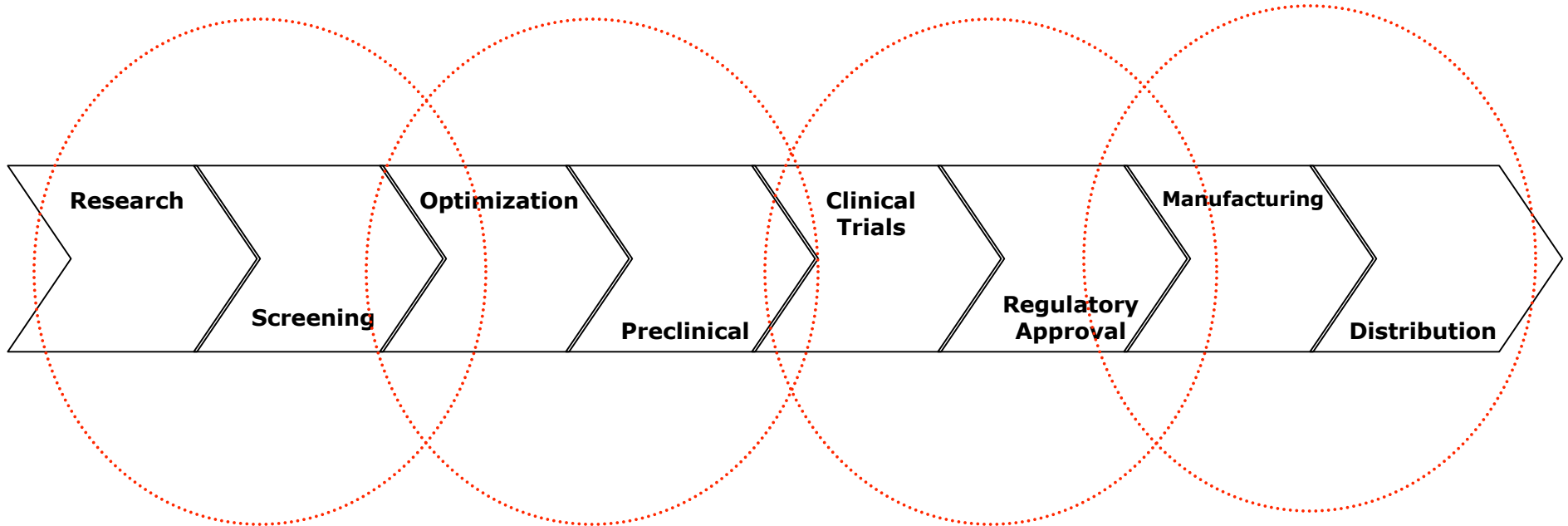
- **Chemical Stability** - Can the compound stand up to extreme tropical conditions?
- **Affordability** - How much does the treatment cost? Is this an improvement?
- **Global impact** - How pervasive is the problem? How debilitating is the disease?
- **Ethics** - How were the clinical trials conducted? What research principles were followed?

# The Need for Complementary Skillsets

The 8 key steps any pharmaceutical development require 4 key skillsets:

*1. Basic Research*

*3. Market Access*



*2. Commercialization*

*4. Sales and Supply Chains*

# Explaining the Glacial Progress

*Take a closer look at the four skillsets and a pattern starts to emerge - especially for neglected diseases:*

- Basic Research
- Commercialization = **Areas of PRIVATE SECTOR expertise**
- Market Access
- Sales and Supply Chains = **Areas of PUBLIC SECTOR expertise**

Partnerships in the 20th Century tended to **FAIL** because they got this essential reality backwards: **They focused public sector resources on stages (1) and (2), and left their private sector partners to deal with stages (3) and (4)**

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# The Transformative Role of Bill Gates

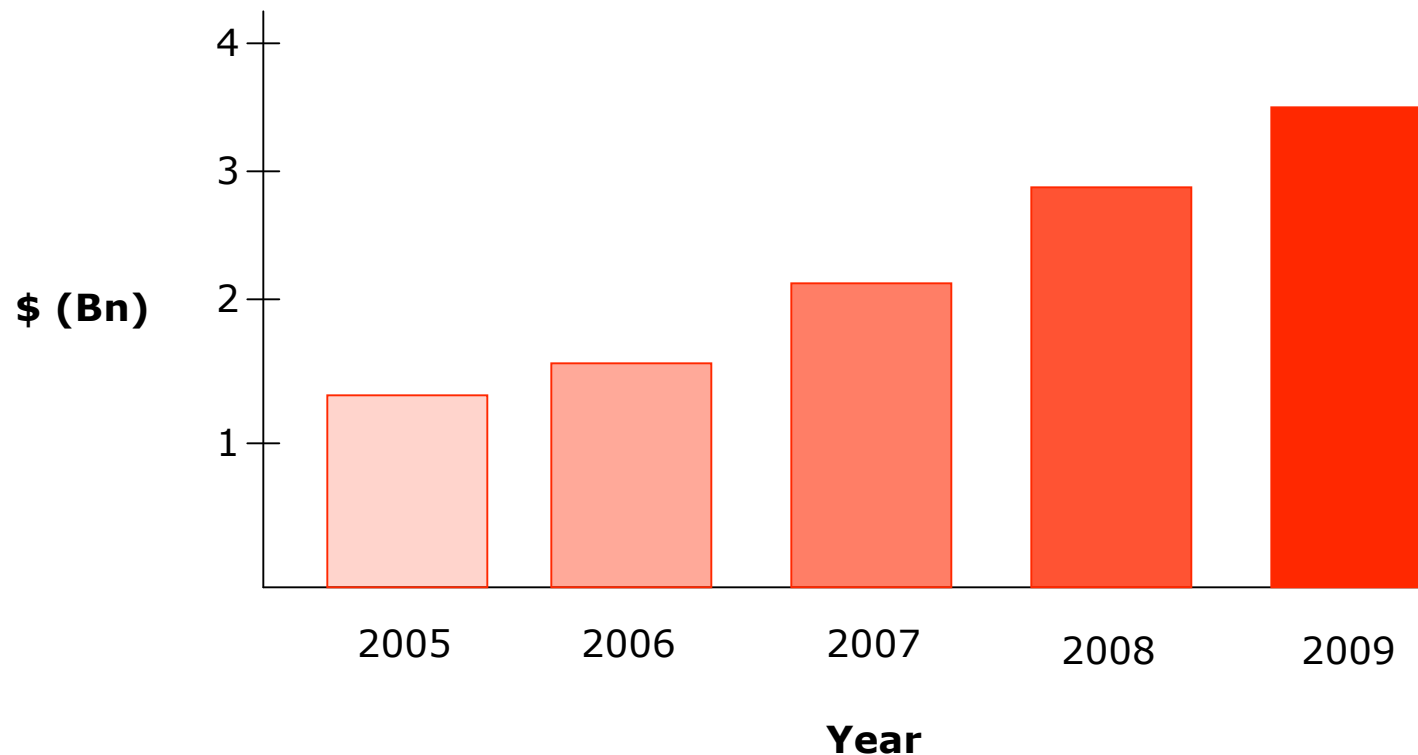
*In the past 10 years, the emergence of the Gates Foundation has completely changed every aspect of global health - including neglected diseases:*

- Gates brought a technology entrepreneur's mindset to the global health space
- In the neglected disease space, his background **allowed** him to help diagnosis some of the market dynamics preventing the creation of a new generation of pharmaceuticals
- His **wealth** allowed him to invest in an emerging set of institutions determined to learn from earlier mistakes and turn a failed public-private partnership model upside down

**Since making global health a core program area in 2000, the foundation has invested over \$7.8 billion on the sector.**

# An Unprecedented Scale of Funding

*Even before Warren Buffet's decision to leave the bulk of his fortune to the Gates Foundation, it was giving away billions of \$ a year. That gift will double the Foundation's granting over from 2006-2009:*



## The Impact

Although much of the critical early thinking came from the **Rockefeller Foundation**, the level - and focus - of the **Gates Foundation's** spending on neglected diseases is the single biggest factor behind the emergence of this new breed of public-private partnerships.

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# A New Age

Since 2000, the neglected disease landscape has changed ***dramatically***:

- At the end of 2004, **61 neglected disease drug development projects** were in progress, and since then at least another dozen are approaching launch.
- 18 products are in clinical trials, ½ of which already in Phase III.
  - *Phase III = randomized, controlled trials on large patient groups ranging from 300-3000*

.....
- Assuming sufficient funding – and standard attrition rates – there should be **no fewer than 8-9 new drugs coming to market over the next 5 years.**
- In the past two years alone, new drugs have been approved to treat both Malaria and VL.

.....
- This new activity is at a level unheard of in the past 2 decades.
- AND it's happening in the absence of significant new government incentives.

**So what's going on???**

# The Rising Role of Multinational Corporations

*MNCs are now involved in more than 1/2 the neglected disease drug development projects*

- Since 2000, MNCs have been critically important to the success of PPPs.
- Companies are now developing promising new disease leads, taking them to point of clinical development and then looking for public partners to help fund further development - this is a reversal of 10-15 years ago.
- PPPs and MNCs can then partner for the key approval and delivery stages:
  - PPPs bring developing country and neglected disease knowledge and skills - and assistance with developing country regulatory approval.
  - MNC prepare and guides regulatory submissions, and takes responsibility for manufacturing and distribution (either themselves or via a generic pharmaco).

# The Rising Role of Multinational Corporations

4 MNCs now have formal neglected disease divisions:



- In EVERY case, MNCs are working on a “no profit, no loss” basis. **Why?**

***“This approach is driven by longer-term business concerns, including managing reputational risk, addressing ethical issues and strategic positioning in growing LDC commercial markets.”***

Dr. Mary Moran - LSE/Wellcome Trust

# The MNC Perspective

*From the MNC perspective, pre-2000 and post-2000 are completely different eras:*

## **Before 2000:**

- Government R&D policies and incentives were generally created around a belief that public institutions would oversee the search for promising drug leads - and then MNCs would become involved in later-stage clinical research and clinical trials, including large-scale clinical trials in developing countries.
- This is VERY expensive for industry:
  - Not only are the associated liability risks huge, but emerging market clinical trials are an area in which most Western-focused companies have little or no experience.
- Most companies responded to these risks by retreating from neglected disease R&D entirely - or by focusing primarily on less risky and costly “adaptive R&D” = reformulations, re-registrations or new combinations of existing drugs.
- Unsurprisingly, the results were generally poor.

# The MNC Perspective (cont)

## Since 2000 all of this has changed:

- Most MNCs have now switched their focus to early pipeline R&D.
  - Three new institutes have been formed at AZ, Novartis and Sanofi-Pasteur dedicated solely to neglected diseases (and complementing the GSK lab that already existed).
- Companies are now developing promising new disease leads, taking them to point of clinical development and ***then*** looking for public partners to help fund further development.
  - Public partners are also essential for assisting with developing country clinical trials.
- The two sides then work together to trial, register and distribute the final drugs:
  - The public partner provides developing world and neglected disease knowledge and skills, and assistance with surmounting regulatory hurdles.
  - MNCs prepare the regulatory submissions and assume the manufacturing and distribution role - using the supply chain knowledge of their partners.
  - **MNCs may also work with generics to produce the final product - one of the rare instances of collaboration.**

# Why the Model Works

- This new approach is unique because it relies heavily on presence of public partners who can help companies take promising leads through to development and delivery.
  - Prior to 2000, the WHO's TDR program was the only entity with the skills and mandate to play this role.
- This new approach is attractive to companies since it requires far less downstream investment - and since it doesn't leave companies trying to manage the risks inherent in large-scale clinical trials thousands of miles from the HQs.
- These lower costs allow companies to offer any resulting drugs at **"no-profit, no-loss" prices** (I.e., at or near the cost of production).
- This has 3 advantages:
  - It encourages companies to become source of high-quality innovative drug leads.
  - It leverages public skills in exactly the area where their impact is essential.
  - It provides innovative products to poor patients at far more affordable prices.

**But MNCs aren't the only corporate partner in town...**

# Small Companies, Big Opportunities

*Small drug companies - including some firms in the developing world - are also becoming involved in the neglected disease space:*

- 29 of the 61 formal projects underway at the end of 2004 were being spearheaded by small pharmacos.
- However, small firms working in the neglected disease space are in fact driven by **commercial motivations** – which means public sector partners need to approach them with an entirely different set of incentives.
- There are 2 main types of firms involved:
  - Some companies (most likely Western) see the neglected disease market as sufficiently commercially attractive, especially for to larger markets like those for TB and malaria.
  - A second group (most likely from emerging economies) consists of small firms using neglected disease R&D to support their primary Western commercial focus.
- Unlike MNCs though, both groups of firms will require their relevant PPP to provide comprehensive support for their involvement in the venture - including significant developing country technical assistance.
- Finally, some contract-research organizations (CROs) see the neglected disease space as an interesting niche sector.
  - CROs are now involved in ~1/3 of current PPP projects on a full-cost commercial basis.

# The Importance of Sustainability

*Since small companies are not motivated by corporate social responsibility concerns, they are potentially a more reliable partner:*

- Though laudable, the altruistic impulse of MNCs can be subject to the vagaries of capital markets and quarterly reporting.
- However, most small companies lack the ambition and the funding to actively participate in this space.
- And once a commercial dimension is introduced into the PPP relationship, issues like intellectual property rear their ugly head - injecting an enormous challenge into the dynamic.
- Unfortunately, these challenges are exacerbated by the fact that current public R&D incentives are also poorly suited to small company needs - and without considerable financial support from either a national government or from the PPP itself, most small companies won't be able to participate.

# The Essential Role of PPPs Themselves

*Contrary to popular belief, PPPs do not in fact conduct drug development themselves. Instead, they have 3 main functions:*

- **Integrate** and coordinate multiple industry and academic/research partners and contractors along the entire drug development pipeline.
- **Distribute** philanthropic and public funds to R&D projects with sufficient public good to justify their support.
- **Manage** neglected disease drug portfolios by accelerating or ending projects based on their potential impact.

# The Essential Role of PPPs Themselves

*Despite their individual characteristics, PPPs tend to offer three generic benefits:*

- **First**, they increase the efficiency of government spending on R&D - while simultaneously helping to select those projects behind which funders should throw their support.
- **Second**, they can search multiple sources for the most promising drug development leads, from MNCs to universities to public sector research labs.
- **Third**, they can leverage the skills and cost savings offered by developing country manufacturers to reduce overall drug development pipeline costs.

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- The Last 5 Years
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    - Medicines for Malaria Vaccine
    - TB Alliance
  - Big Questions
  - Recommendations
  - Conclusions

# The Age of PPPs

*Since 2000, a new generation of public-private partnerships (PPPs) has revolutionized drug discovery:*

- PPPs are involved in 47 of the 61 neglected disease drug development projects formally underway at the end of 2004.
- The 4 innovative PPPs that formed the basis of my research have emerged in the last 7 years alone:



# Making a Difference

## Drugs for Neglected Diseases Initiative

- DNDi emerged out of *Médecins sans Frontières*' "Access to Essential Medicines" campaign.
- Its unique approach is based on partnering research institutes in the developing world.
- **In March 2007, DNDi unveiled ASAQ - a new once-a-day fixed dose malaria product that will be available for a full treatment cost of \$0.50/child and \$1.00/adult.**

## Global Alliance for TB Drug Development

- Founded in 2000, the TB Alliance has 9 products in the discovery stage and three drugs in clinical trial - products that would replace existing drugs that are 40 years old.
- The Alliance is working closely with a range of pharmacos, in particular GlaxoSmithKline and Bayer.

## Medicines for Malaria Venture

- With 30 projects in its portfolio, MMV expects to have 4 new fixed-dose Artemisin Combination Therapies (ACTs) on the market in the next 3 years.
- MMV works with 87 partners in 33 countries - **but no organizations in Canada.**

## Institute for OneWorld Health

- In August 2006, OneWorld had its first drug approved by the Drug Controller General of India.
- The drug - a Parmomycin IM injection - was approved for use against Visceral Leishmaniasis.
- Remarkably, the drug was approved only 3 months after it was submitted - reflecting the in-country knowledge of One World's Hyderabad-based manufacturing partner Gland Pharma.
- **Gland will make the medication available at cost - or approximately \$10/treatment (far less than the \$30-300 price of existing treatments).**

*Case Study #1*

# **Drugs for Neglected Diseases Initiative**

# DNDi

## *History and Mission*

- The foundation for DNDi was laid in 1999, when *Médecins sans Frontières* (MSF) brought together a group of neglected disease experts.
- This group formed the Drugs for Neglected Diseases working group - a loose network that would go on to launch both DNDi and MSF's "Access to Essential Medicines" advocacy campaign.
- DNDi is a not-for-profit organization, based in Geneva, focused on assembling a pipeline of promising drug candidates.
- Initially, the organization is focusing on three diseases:
  - Chagas
  - Visceral Leishmaniasis
  - Sleeping Sickness
- DNDi explicitly articulates its mission as taking on the projects others are "unwilling or unable to do".

# DNDi

## *Funding & Budget*

- Many PPPs working in the neglected disease space rely on a single funder for the bulk of their support.
- Most often this funder is the Gates Foundation - but in DNDi's case, it's MSF itself, the organization from which DNDi sprang.
- MSF has committed sufficient funds for DNDi to operate for its first 5 years - a period that will end in late 2008.
- DNDi has also been actively seeking support from foundations, national governments, research agencies, international organizations and other public sector entities.
- Not counting its drug portfolio project costs - which climb from \$4 million a year in 2003 to \$24 million in 2014, DNDi runs a tight ship:
  - Its annual operating budget was only \$3.5 million - and that covers headquarters and four regional offices.

# DNDi

*Registered in 2003, DNDi was formed by 6 public sector research partners - each of whom has a profound "social mission" that appeals to DNDi:*

- *MSF*
- Oswaldo Cruz Foundation/Fiocruz (Brazil)
- Indian Council of Medical Research (India)
- *Institut Pasteur* (France)
- Ministry of Health (Malaysia)
- Kenya Medical Research Institute (Kenya)

Although DNDi works closely with private sector firms - most notably **Sanofi-Aventis** - it has a very deliberate orientation toward the public sector, from both strategic and financial perspectives.

# DNDi

## *Strategy*

- DNDi's model is based on matching patient needs to gaps in the drug development pipeline.
- In other words, it focuses on researching drug leads that would fill one of the treatment gaps that currently exists in the therapeutics available for its target diseases.
- There are three key stages where DNDi focuses its attention:
  - o At the early discovery stage
  - o At the stage before drugs enter clinical development
  - o At the stage when drugs should reach affected populations but they do not

**DNDi's pipeline is robust.** As of January 2007, it had identified 20 projects: 10 in the discovery phase, 4 in preclinical development and 6 in clinical trials.

# DNDi

## *Impact*

- In March 2007, DNDi unveiled ASAQ - a new once-a-day fixed dose malaria product that will be available for a full treatment cost of \$0.50/child and \$1.00/adult.
- Manufactured by Sanofi-Aventis, ASAQ was registered in Morocco, with formal approval granted on February 1 of this year.
- Six years after the WHO recommended the use of artemisinin-based combination therapies, the first AS-AQ fixed dose therapy is now available (AS = artesunate; AQ = amodiaquine - two antimalaria medications that are far more effective when taken together)
- The potential impact of ASAQ is profound:
  - Rapid effect
  - **A cure rate of over 90%**
  - Fewer tablets to swallow, shorter course of treatment
  - Doses designed for both adults and children
  - **Cheaper than existing combination therapies**

*Case Study #2*

# **The Global Alliance for TB Drug Development**

# TB Alliance

## *History and Mission*

- The TB Alliance emerged out of a meeting held in Cape Town, South Africa in February 2000.
- The gathering - attended by more than 120 leaders from academia, industry, NGOs, agencies and donors - made the case for a new, accelerated framework for TB drug development.
- The Alliance was formally launched 8 months later at the International Conference for Health Research for Development in Bangkok, Thailand.

# TB Alliance

## *Funding and Budget*

- Gates Foundation is a major funder of the Alliance (over 70% of total funds). However, a number of national development agencies and foundations are making major contributions:
  - o The Rockefeller Foundation
  - o The UK Department for International Development (DFID)
  - o US Agency for International development (USAID)
  - o The Netherlands Ministry of Foreign Affairs
  - o Irish Aid
- Since its inception in 2000, the Alliance has received almost \$200 million in funding - but estimates it still faces **a funding shortfall of at least \$100 million.**

# TB Alliance

## *Partners*

- **Industry**

- o Bayer
- o Cumbre
- o GSK
- o Korea Research Institute of Chemical Technology
- o Novartis

- **Academic**

- o National Institute of Allergy and Infectious Diseases (US)
- o University of Auckland (New Zealand)
- o University of Illinois - Chicago (US)
- o Yonsei University (Korea)

- **Key Stakeholders** include:

- o The Gates Foundation
- o The European Commission
- o The Global Fund
- o MSF
- o Treatment Action Group
- o US Centres for Disease Control
- o The Wellcome Trust
- o The World Bank

# TB Alliance

## *Strategy*

- The Alliance's strategy is referred to as the "3As," for affordability, adoption and availability
- Its business model is that of a fairly traditional PPP:
  - It combines the R&D expertise of its staff with complementary skillsets found in industry and government partners, and operates as a largely virtual organization to keep its costs down.
- The Alliance's currently has 11 projects in its development portfolio. 2 are in Phase II clinical development, while the remaining 9 are split between the "Identification" and "Optimization" stages of Discovery.
- In addition to its drug discovery work, the Alliance is also working on clinical trial site assessments, biomarker identification and generating a mouse model of TB.

# TB Alliance

## *Impact*

- Although the Alliance has yet to bring a new product to market, its impact can already be felt through its work on improving clinical trials infrastructure.
  - The new paradigm being developed would assess each drug compound individually through Phase I clinical trials - while simultaneously evaluating potential combinations in preclinical models.
- The Alliance is also working with key regulatory authorities - the Food and Drug Administration (US), the EMEA (Europe) and authorities in South Africa and Brazil - to develop new guidelines for TB drug registration and approval.
  - It is also using Open Forums to bring together regulators, industry representatives, academic researchers and public health and patient advocates.
- The need for new products is acute, since the **last major TB therapeutic discovered and brought to market - Rifampicin - came on-stream in 1963.**

*Case Study #3*

# **Medicines for Malaria Venture**

## *History and Mission*

- Established as a foundation in late 1999, MMV emerged out of discussions between the WHO and the international association representing the world's major pharmaceutical companies - the International Federation of Pharmaceutical Manufacturers Associations.
- Although MMV has since brought in a number of key stakeholders, its **founding is unique both for the bilateral nature of the discussions, and for the central role played by a major industry player in the organization's inception.**
- This may reflect the size of the malaria market - since DNDi and OneWorld (both PPPs focusing on diseases that have been even more neglected - have experienced far less strategic interaction with corporate partners).

# MMV

## *Funding and Budget*

- Since 1999, MMV has received over \$273 million in funding and pledges.
- \$152 million has been received and spent already - leaving \$121 million outstanding.
- The Gates Foundation is again the single largest donor (60.5%), followed by the UK DFID (10.6%), the Wellcome Trust (9.6%) and the Netherlands Minister Development Corporation (6.2%)

**On the expenditure side, 91.2% of the \$51.5 million collected in 2006 went to project related R&D - a total of over \$47 million. Management and Administration was 6.8%, or ~\$3.4 million.**

# MMV

## *Partners*

- MMV works with partners in 33 developed and developing countries - but **no Canadian institutions**
- Key partners include:
  - o The Rockefeller Foundation
  - o Global Forum for Health Research
  - o Swiss Agency for International development
  - o The World Bank
  - o The Wellcome Trust
  - o The National Institutes of Health
  - o The Association of the British Pharmaceutical Industry

- o Hofmann-Laroche
- o Novartis
- o GSK
- o Genzyme

# MMV

## *Strategy*

- MMV's portfolio of drug discovery projects is filled with 30 projects - the largest assembly of anti-malarial drug leads in history.
  - o 19 of the projects represent completely new classes of drugs.
  - o 9 projects comprise a mini-portfolio administered by the Novartis Institute for Tropical Diseases.
  - o Another 5 are clustered around a research partnership that links between the Broad Institute of MIT with Harvard and Genzyme.

**MMV's ultimate goal is a one-dose cure.**

# MMV

## *Impact*

- 2006 saw MMV broaden its strategic focus and expand its potential impact by adding a “deliver” component to the “discover” and “develop” that had been the foundation of its previous activities.
- The organization’s disease focus is also expanding, as it partners with Novartis to specifically target a marginalized strain of malaria known as *plasmodium vivax* malaria.
- 2006 saw more than 3000 patients enrolled in clinical trials in 40 research centres spread across 20 countries - with the focus the 4 new artemisinin-based combination therapies (ACT) in Phase III.

**With 5 of its projects in Phase, MMV should be receiving regulatory approval for its first product success before 2010.**

*Case Study #4*

# **The Institute for OneWorld Health**

# OneWorld

## *History and Mission*

- One World is the first nonprofit pharmaceutical company based in the United States.
- The company began as a strategic plan written by now-CEO Dr. Victoria Hale in 1998, who proceeded to invest her own seed capital to get the venture off the ground.
- OneWorld was incorporated in 2000 and received its tax-exempt 501(c)(3) Status the next year.
- In 2002, the company received two Gates grants and began to garner global attention.
- Piggy-backing on the first neglected disease PPP, **OneWorld signed a collective licensing agreement with the WHO's Special Programme for Research and Training for Tropical Disease in 2003.**
- Over the last four years, the company has accumulated patents and drug leads, received significant foundation support and developed a deep set of corporate and academic partners.

# OneWorld

## *Funding & Budget*

- Like many of its peers, OneWorld is strongly supported by the Gates Foundation:
  - **Since 2002, the Foundation has awarded grants totaling over \$100 million.**
  - Regina Rabinovich - the Gates Foundation's Director of Infectious Diseases - also sits on OneWorld's Board.
- OneWorld also has a surprisingly robust set of individual donors: its website records those who donated even up to \$250, a list that numbers almost 200 names.
  - Those who donate \$250-1000 or over \$1000 were also listed.
- **Compared to other PPPs, OneWorld is therefore much more integrated into its local philanthropic community - perhaps in part because of the US' strong tradition of charitable giving.**
- Interestingly, more detailed information on the company's financial operations is quite difficult to find.

# OneWorld

## *Partners*

- Industry
  - Amyris Biotech (US)
  - BioFocus DPI (UK)
  - Gland Pharma (India)
- Governments and NGOs
  - Indian Council of Medical Research (India)
  - International Centre for Diarrheal Disease Research (Bangladesh)
  - National Institute of Cholera and Enteric Diseases (India)
  - Odyssey Research (US/India)
  - World Health Organization Program for Research and Training in Tropical Diseases (Switzerland)
- Academic
  - Balaji Utthan Sanastan Research Centre (India)
  - Centre for Health and Population Research (Bangladesh)
  - Dr. A.K. Aditya Clinic (Bihar)
  - Kala-azar Research Centres (India)
  - Massachusetts General Hospital (US)
  - Rajendra Memorial Research Institute (India)
  - Research Centre for Diabetes, Hypertension and Obesity (India)
  - Shrimati Hazari Maternity and Medical Care (India)
  - University of California, Berkeley
  - University of Georgia

# OneWorld

## *Strategy*

- OneWorld's approach is based on challenging the assumption that neglected disease R&D is too expensive to create a new generation of transformative products.
- To reshape the drug development paradigm, OneWorld relies on 3 key ingredients:
  - Donated intellectual property
  - Partnering with industry and academic researchers
  - Creating global manufacturing and supply chains to leverage developing world expertise - and reduce development costs
- This focus on donated IP is a relatively unique feature of its operations.
- Referring to the pharmaceutical industry breakdown on **slide 39**, OneWorld is not involved in stages 1 or 2 ("Research" and "Screening") nor is it involved in stages 7 or 8 ("Manufacturing" and "Distribution").

**Instead, the company operates at the heart of the drug development process - stages 3-6: "Optimization," "Preclinical," "Clinical Trials," and "Regulatory Approval."**

# OneWorld

## *Impact*

- OneWorld embarked on the world's largest Phase III clinical trial for VL in 2003. The trial took place in India, and was completed the next year.
- In August 2006, OneWorld had its first drug approved by the Drug Controller General of India, a Parmomycin IM injection approved for use against VL.
- Remarkably, the drug was **approved only 3 months after it was submitted** - reflecting the in-country knowledge of One World's Hyderabad-based manufacturing partner Gland Pharma.

**Gland will make the medication available at cost - or approximately \$10/treatment** (far less than the \$30-300 price of existing treatments).

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**Although PPPs have had a revolutionary impact, some big questions remain...**

# (1) Where is the “Steve Jobs” of global health?

- The influence of the Gates Foundation on the neglected disease space has been profound - and profoundly positive.
- And yet, the sheer volume of funds being invested by a single entity can “crowd out” important policy debates and obscure vital differences of opinion.
- Although another institution able to invest \$916 million on global health - as the Foundation did last year - is unlikely to emerge overnight, it is important to find ways to support a diversity of voices and perspectives around these key issues.

**One Canadian - and Torontonionian - who could potentially play this role is Dr. James Orbinski.**

# The Influential Role of Dr. James Orbinski

*In addition to his role as a Board member of both the TB Alliance and DNDi, Dr. James Orbinski is also connected to at least two other international organizations playing instrumental roles in global health:*

- **Dignitas** - The mission of Dignitas is to provide a quality of life for families and children living with HIV/AIDS in developing countries. Orbinski is Dignitas' chair.
- **Médecins Sans Frontières** - MSF is one of the world's most effective and long-standing global health and development organizations. Its "Access to Essential Medicines" campaign has been a vital counterpart to the work that DNDi and others have been doing on the pharmaceutical side. When MSF won the Nobel Peace Prize in 1999, Orbinski accepted the award on the organization's behalf.

DIGNITAS



## (2) Which model looks best? “Push” or “Pull”?

- Traditional PPPs are based on the “**push**” model - creating a new collaboration to enhance the supply of new pharmaceuticals
- So-called “Advanced Market Commitments” on the other hand represent the “**pull**” model:
  - o An AMC is a promise by a funding agency or foundation that it pay \$X/tablet for Y million tablets of a new drug to treat chagas, for example
  - o Companies - or PPPs - then compete amongst themselves to produce the fastest and most effective product that meets the funder’s criteria.
  - o AMCs eliminate demand uncertainty - while also taking the onus off the funder to determine just which project looks the most promising at each stage of the drug discovery pipeline.
  - o According to the Gates Foundation’s Girindre Bihari, AMCs represent “the most important development in the neglected disease space in years”.
- Despite their appeal, however, AMCs are at their very earliest stage of development - and may prove more effective in the vaccine space.

### (3) Is the PPP model sustainable?

- Some influential thinkers working in the global health space are starting to question the sustainability of the MNC-driven PPPs.
- In their place they propose two alternatives:
  - A neglected disease R&D pipeline model that's entirely funded by the public sector - in which the elimination of intellectual property issues creates a huge incentives for collaboration.
  - A hybrid PPP model in which developing country firms play an increasingly important role - as MNCs begin to recede in relevance and utility.
- And yet neither approach addressed the biggest challenge to PPPs - the cost to bring even a single drug to market
  - **Even with through a PPP, pushing a single compound all the way through to distribution will cost ~\$100 million.**

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## Bring Industry Expertise into Universities

- The issue of commercialization lies at the heart of much of the analysis of the efficacy of PPPs.
- PPPs work when they combine company experience in bringing ideas to market with public sector experience in clinical trials and regulatory approval.
- Given these respective strengths, building closer academic-corporate ties may be a way to mirror some of these PPP successes.

**Spotlight:** *Centre for Interdisciplinary Research, The University of Dundee (SCOTLAND)*

The Centre is the recipient of £8.1M Technology Transfer Strategic Award from the UK-based **Wellcome Trust**, one of the world's leading health analysis and advocacy organizations.

Under the leadership of Professors Mike Ferguson and Alan Fairlamb, the Centre is setting up a drug development programme within a university environment - and then staffing it with scientists and researchers coming out of industry.

## **Match Foundation Funding with Public Funding**

- Despite their impact, relatively little public money is given to PPPs
- In the five years to 2004, only four members of the OECD - the United Kingdom, the US, the Netherlands and France - contributed to PPPs.
- This ongoing lack of public support - accompanied by minimal efforts to educate citizens about the effectiveness of PPPs - has the potential to fatally weaken this new class of PPPs.
- This scenario would force governments to look elsewhere for their early-stage drug discovery product leads - or to embark on the costly and bureaucratic task of building a research capacity in-house.
- Instead, governments should create a "matching pool" to support innovative approaches to solving global health challenges.

## And yet....

- PPPs receive very little public \$ (*as opposed to private philanthropic support from the Gates Foundation and other*)
- 30 OECD members – whose economies generate a collective GDP of US \$30 **trillion** a year – have contributed only US \$43 million to drug development PPPs in the five years to 2004.
- As a result, PPPs entered 2005 with a shortfall of 40% - a shortfall that has only grown over the last two years.

**And Canada is nowhere to be seen**

- There are also no public policies in place specifically to underwrite industry's current participation in PPPs - or to encourage their future participation.

## **Recognize Industry's New Role**

- Policymakers have been slow to recognize the rise of multinational corporations as a key players in the neglected disease space.
- This needs to change, since MNCs have the diversified compound libraries and the early-stage drug discovery expertise required to accelerate the search for new diagnostics and therapeutics.
- Four companies have dedicated neglected disease research centres - Novartis, Sanofi-Aventis, GSK and AZ. Although these companies should be commended, their peers need to be challenged to demonstrate a similar degree of commitment.
- An increased willingness by politicians and policymakers to highlight these positive examples - perhaps as part of global for like the World economic Forum or the Clinton Global Initiative - would dispel some of the negativity surrounding "big pharma" while further incenting the pharmaco hold-outs to reconsider the degree of commitment to neglected disease R&D.

## Be Wary of Compulsory Licensing

- “Compulsory Licensing” allows countries to break international patents and replace branded drugs (usually imported) with generic equivalents (often domestic).
- Under the agreement on TRIPS - or “trade-related aspects of intellectual property rights” - CL is only allowed under special circumstances such as national health emergencies (and only then after efforts to negotiate prices with firms).
- The World Health Organization and major global health players - like the Clinton Foundation - argue that CL will lead to more cheap drugs reaching the global poor.

### ***But the issue of CL is much more complicated than it first appears...***

- The countries using CL most often are **not** the impoverished nations of sub-Saharan Africa
  - **These countries get the bulk of their drugs either free or at nominal costs**
- Instead, the countries turning to CL are middle-income nations with sizable middle classes: Brazil, India and Thailand, to name 3

## Be Wary of Compulsory Licensing (cont)

- The result is that citizens in middle-income countries may be able to access medicines more cheaply than their counterparts in the developing world.
- CL may also drive industry players out of the neglected disease space entirely - when the success of PPPs suggests the solution is in fact **more** industry involvement.
- This is a view shared by both **Tadataka Yamada of the Gates Foundation**, and the **Institute for OneWorld Health's Victoria Hale** - two of the leading figures in the fight against neglected diseases....

### ***So is there a better way?***

- Companies should instead develop a sliding scale, linking price to a universally accepted indicator of economic development, like *GDP per capita*.
- This approach would see the most marginalized populations in the poorest countries benefit from the cheapest prices - and avoid the complexities that occur when governments of middle income countries (with the means to increase their health expenditure) instead pursue CL as an increasingly common policy instrument.

## **Create a “Neglected Disease Innovation Fund”**

- The Canadian Institutes for Health Research is this country’s principal health care research funder.
- Although CIHR has a number of innovative funding, training and exchange programs with a global health component, there are no funding pools dedicated solely to commercializing Canadian innovation that has the potential to impact global health.
- Launching such a fund - and giving it resources in the neighbourhood of \$100 million over 5 years - would immediately signal to foundations, companies, universities and PPPs themselves that Canada is committed to making a significant contribution to the battle against some of the world’s most intractable pandemics.

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# Transformative Impacts

- As the preceding slides hopefully demonstrated, a new breed of PPPs has emerged over the past 7 years and completely transformed the neglected disease landscape.
- I reached this conclusion as part of another transformative period - the last 16 months that I've spent as a Gordon Foundation Global Youth Fellow.
- I feel profoundly fortunate to have had the opportunity not only to work on this project, but to have been part of the inaugural year of unique national experience whose impact I'm only now beginning to realize.
- So let me close by simply saying thanks - to the Foundation, to Patrick and Marjan, to my fellow Fellows and to the dozens of individuals who shared their time, their insights, their enthusiasm and their coffee with me.
- This has been a hard project to put down, and one I know I'll carry with me for a long time as I move on to other personal and professional challenges - and that, I am utterly convinced, is exactly the point.

## **Ross Wallace**

Walter and Duncan Gordon Foundation

Global Youth Fellow (2006-7)

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Director, Strategic Partnerships

MaRS Discovery District