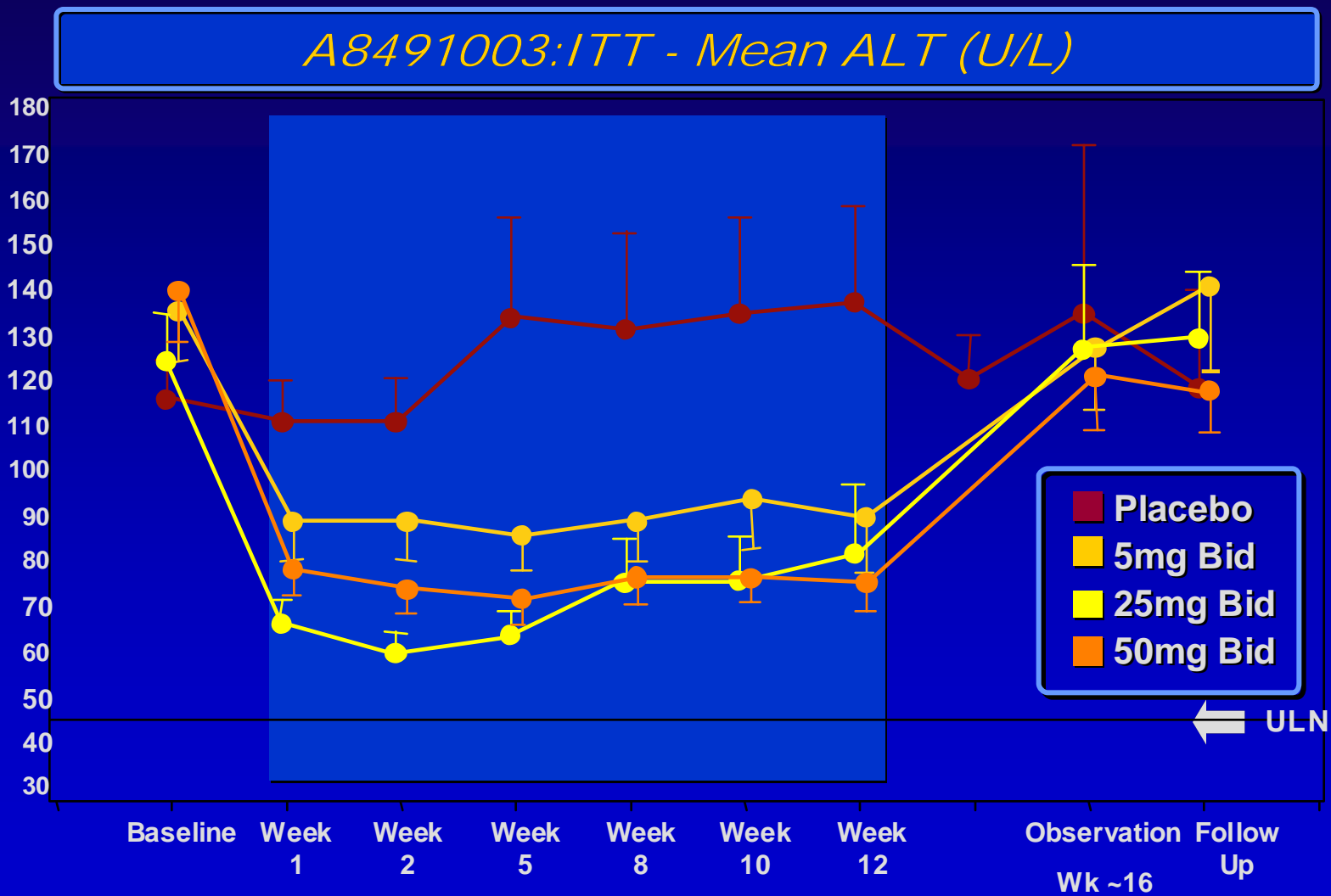




# PF-3,491,390 Pan-Caspase Inhibitor





# Antibacterials Strategy

| Sector/<br>Disease | Concept   |
|--------------------|---|
| Hospital           | Targeted Gram-Negative Infections<br>• <i>Pseudomonas</i> , <i>Acinetobacter</i> , ESBL enterics  |
|                    | Targeted Gram-Positive Infections<br>• MRSA (Methicillin-Resistant <i>Staphylococcus aureus</i> ) |
|                    | Pseudomonas-specific for Problematic Pathogen   |
| Community          | Targeted Respiratory-Tract Infections   |
|                    | Targeted Gram-Positive Infections<br>• Community MRSA for Skin and Soft Tissue                    |
| Host-Targeted      | Prevention of Complications of Sepsis   |



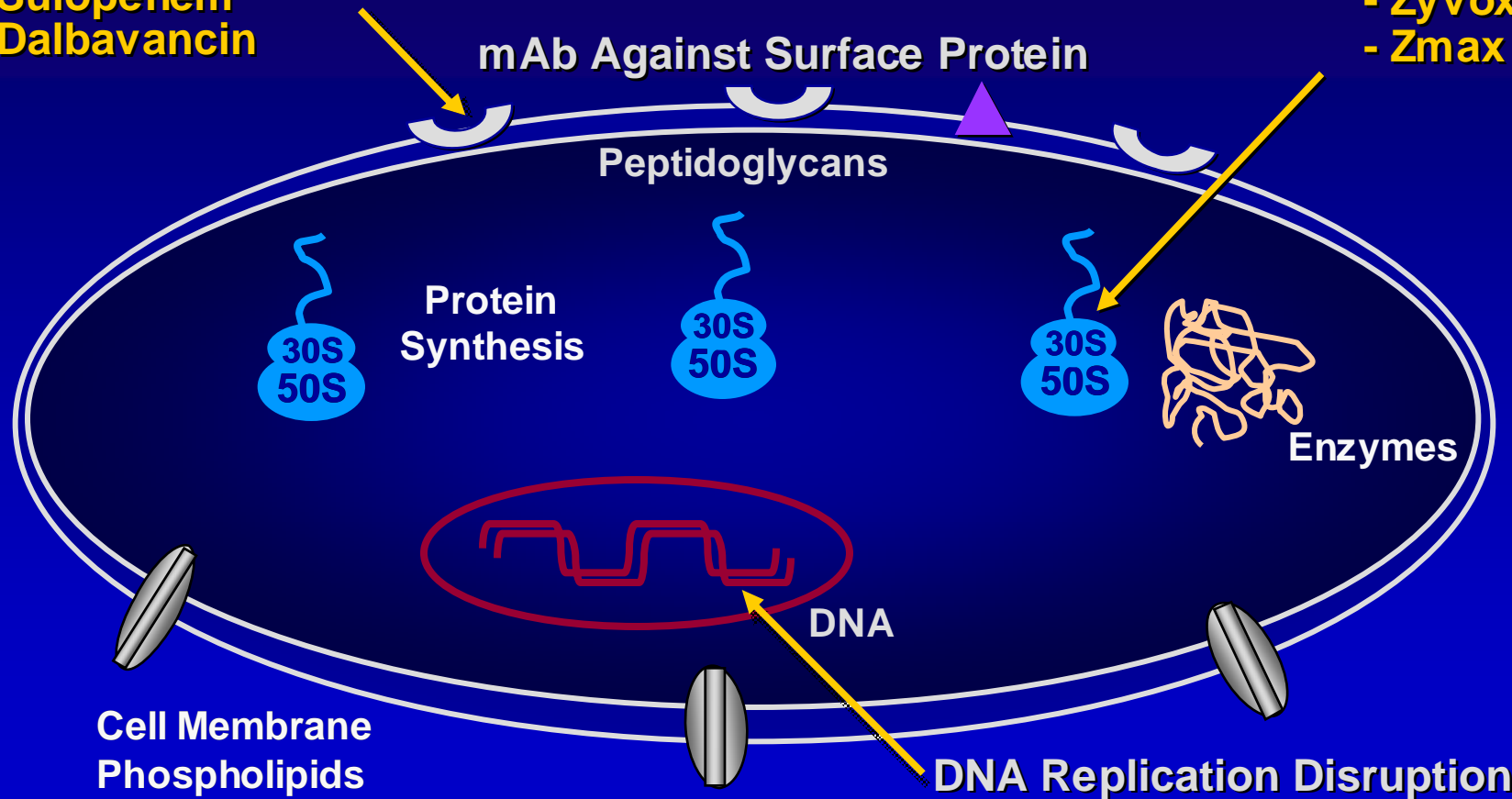
# Antimicrobial Targets

## Cell Wall Inhibitors

- Sulopenem
- Dalbavancin

## Protein Synthesis Inhibitors

- Zyvox
- Zmax



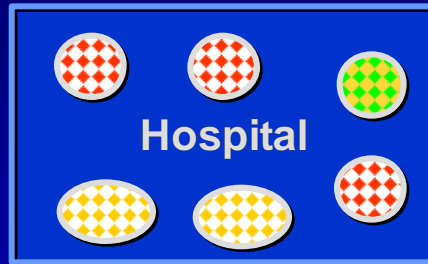
Adapted from Guardabassi et al., Antimicrobial Resistance in Bacteria of Animal Origin. ed. F. Aarestrup. ASM Press 2006.



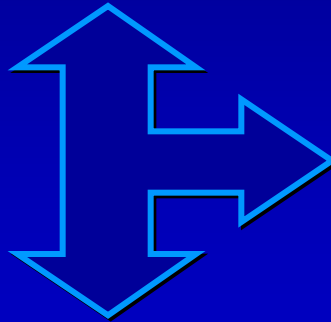
# Evolution of *S. Aureus*

*Hospital - Community Interaction  
Leads to Transfer of Resistance and Virulence Genes*

Antibiotic: **Resistant**  
Virulence: Benign



Antibiotic: **Sensitive**  
Virulence: **Aggressive**



Antibiotic: **Sensitive**  
Virulence: Benign



Antibiotic: **Resistant**  
Virulence: **Aggressive**



## ***Dalbavancin***

***A New Glycopeptide Antibiotic***

### ***Innovative New Antibacterial Therapy***

- ◆ **Highly Effective Against MRSA**
  - **Pharmacokinetic Profile Allows for Once-Weekly Treatment**
  - **Confidence of Intravenous Therapy Without Daily Intravenous Inconvenience**
- ◆ **Potential to Facilitate Early Hospital Discharge and Reduce Overall Treatment Costs**

***1H07 Approval Expected***



# Rapid Diagnostics Enable-Targeted Treatment



*Specimen  
from Patient*

Culture: 24-72 hrs

Rapid Diagnostics: ~ 1 hour



*Pathogen  
Identified*



- ◆ **Timing – Could Emerge in ~5 Years (Multiplex DNA Based)**
- ◆ **Benefits Include**
  - Rapid Prescribing of Appropriate Therapy at the Start
  - More Efficient Enrollment of Desired Subjects for Clinical Studies
    - Estimate that as Many as 70% of Enrollees in Many Antibiotic Studies are not Microbiologically Qualified → Significant Inefficiency



# **PF-3,709,270 (Sulopenem Prodrug)**

## **Cell-Wall Peptidase Inhibitor**

### ◆ **Product Characteristics**

- **Penem Antibiotic with Activity Against Broad Array of Strains**
  - Including Extended-Spectrum Beta-Lactamase Gram-Negatives
- **Orally Bioavailable**
- **Previously Studied in >1,000 Patients While Given IV**

### ◆ **Target Indications**

- **Hospital-Acquired Pneumonia**
- **Complicated Skin Infections**
- **Intra-Abdominal Infections**
- **Community-Acquired Pneumonia**
- **Complicated Urinary-Tract Infections**

### ◆ **Status**

- **Oral-Bioavailability Criteria Met**
- **Clinical Trials on Fast-Track Progression**



## **PowderMed** *DNA Vaccine Company*

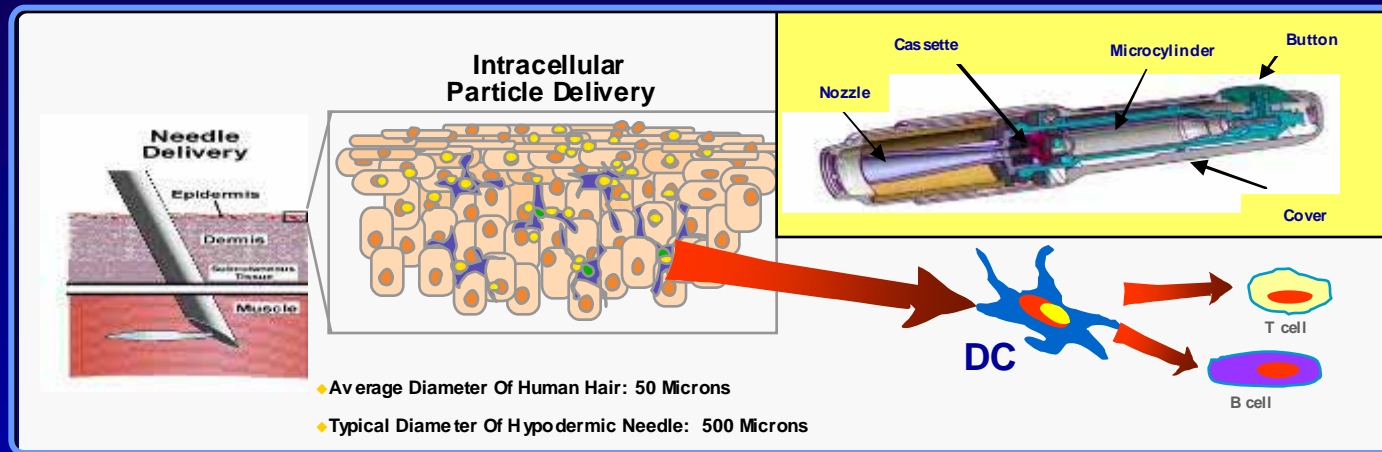
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### ◆ **Rationale For Acquisition**

- **Unique Technology Platform Superior to Competing Technologies**
  - DNA Vaccines Offer Advantages over Traditional and Cell-Based Vaccines
  - PowderMed's Proprietary Technology Offers Additional Advantages
- **Potential For Significant Revenue and Attractive Margin**
  - Vaccine Market is Projected for Significant Growth
  - Increased Awareness and Desire for Preventive Vaccines
  - Specialty Vaccine Could Command Premium Pricing
- **Unique Opportunity as Entry Point for Pfizer Vaccine Strategy**



# Influenza Vaccine



- ◆ **Needle-Free Delivery System**
- ◆ **Delivers DNA-Coated Microscopic Gold Particles into the Skin Using Pressurized Helium Gas**
- ◆ **Elicits Both Antibody and Cell Mediated Immune Responses**
- ◆ **Potential for Improved Efficacy Compared to Traditional Vaccines**
- ◆ **Next Steps**
  - **Work Through Integration of PowderMed Expertise**
  - **Currently in Late Phase 2: Focus on Timing of Phase 3 Start for Seasonal Influenza**



## *Developing World Strategy*





## ***Developing World R&D Strategy***

- ◆ **Focus on Diseases of Greatest Morbidity and Mortality that Need Better Medicines**
  - HIV
  - Malaria
  - Tuberculosis
  
- ◆ **Guiding Principles**
  - Add Value on the Patient's Terms
  - Invest in Research to Synergize with Ongoing Efforts
    - Screen Animal Health Protozoal Portfolio for New Parasitic Agents
  - **Contribute Strengths of Pharmaceutical Enterprise, Including:**
    - Target Selection/Screening/Oversight of Lead Development
    - Project Planning/Regulatory Focus
    - Pharmaceutical Science and Formulation Development
  - Create Transparent Plans to Set Expectations



## **Malaria Burden**

- ◆ **3.2 Billion People at Risk**
- ◆ **Up to 2.7 Million Deaths Each Year**
- ◆ **The Single Greatest Killer of Children in Africa**
- ◆ **350-500 Million Clinical Episodes of Malaria Occur Every Year**
- ◆ **In Sub-Saharan Africa, Malaria:**
  - **Accounts for 40% of Public-Health Expenditures**
  - **30-50% of Inpatient Admissions**
  - **Up to 50% of Outpatient Visits**
- ◆ **Takes  $\geq$ \$12 Billion Each Year From Africa's GDP**

World Health Organization's *World Malaria Report 2005*



# **Zithromax/Chloroquine**

## **Malaria**

### ◆ **Rationale**

- **Azithromycin Weakly Inhibits Malaria Organism but is Well Tolerated and Relatively Safe in Pregnancy**
- **Chloroquine, Although Well Tolerated and Inexpensive, is Decreasingly Effective Due to Resistance**
- **The Combination of the Two Showed Potentiation of Antiparasitic Effects Both in the Laboratory and in a Phase 2 Trial**

### ◆ **Global Clinical Trial Program Initiated**

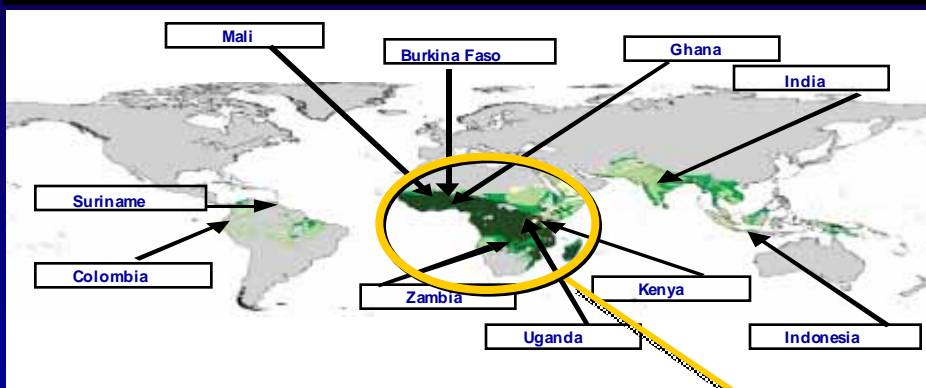
- **Good Activity Seen in India (85% Efficacy) and Excellent Activity Seen in Africa (98% Efficacy) in Combination with Chloroquine**

### ◆ **Plans are for Development of Prevention Indications**

- **Intermittent Preventive Therapy for Pregnant Women and Children in Africa**



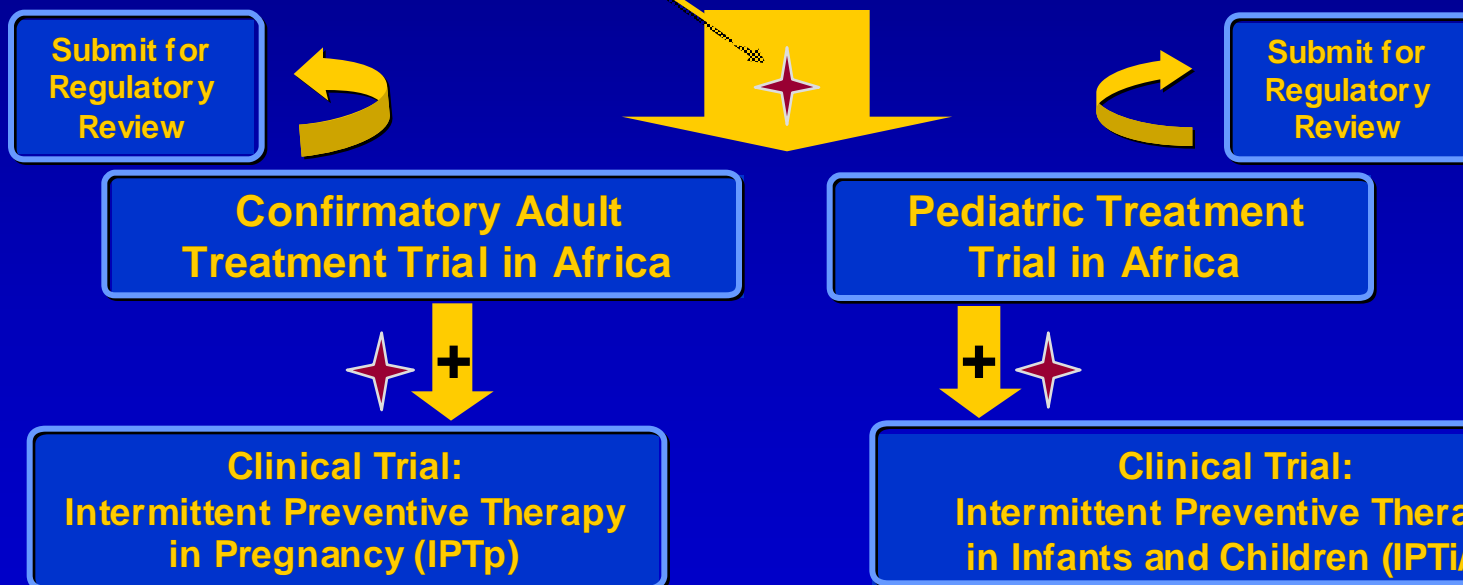
# Zithromax/Chloroquine Targeting Preventive Therapy In Africa



## Phase 2 Conclusions

Regional Efficacy Differences Observed

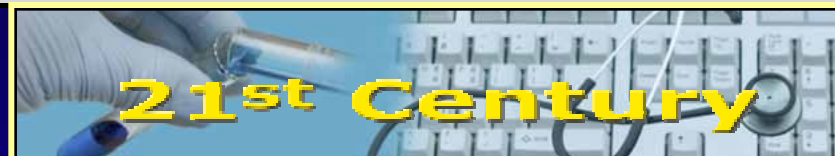
- Excellent Response in Africa
- Dose-Response Seen in India and Colombia
- Combination Well Tolerated



With External Consultation



# Infectious Diseases Therapeutic Area Vision



## ◆ Kill The Bugs



## ◆ Protect The Patient

- Improve Host Immunity
- Emphasize Prevention

## ◆ Delayed Diagnosis

- Best-guess Treatment



## ◆ Rapid Diagnostics

- Immediate, Informed Treatment

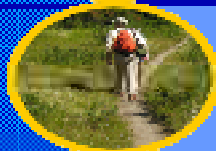
## ◆ Broad-spectrum Agents Drive Resistance And Superinfections



## ◆ Targeted Spectrum

- Precision Therapy

## ◆ HIV Destroys Lives



## ◆ HIV As A Chronic Livable Disease

## ◆ Hepatitis C Virus (HCV) Treatment Worse Than The Disease



## ◆ HCV Cures With No Quality-Of-Life Penalty

## ◆ Research Focused On Pathogen Targets



## ◆ Research Platforms Leveraged Across Other Therapeutic Areas



## **Summary**

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- ◆ **Fifty Years of Experience**
- ◆ **Industry-Leading Breadth and Depth of the Infectious Disease Portfolio**
  - **Re-Affirming and Building on Our Commitment in Anti-Bacterial Therapy**
- ◆ **Moving into New Disease Areas, with New Therapeutic Modalities**
  - **Maraviroc: Ten Years From Idea to NDA**
- ◆ **Portfolio is Being Managed Towards Targeted Therapies in Alignment with Advances in Clinical Medicine and Diagnostic Technologies**
- ◆ **Active Development of Agents for the Developing World**