Challenges in Drug Development in Emerging Markets
Pfizer’s approach to drug development in Emerging Markets

Challenges in drug development for pharma industry
- regulatory
- operational
- compliance
- medical environment

Differences in medical environment: a case study
Pfizer’s Approach to Emerging Markets
Emerging Markets: Mission

Business Unit

We will be recognized for meeting the diverse medical needs of patients in Emerging Markets around the world in an innovative, socially responsible and commercially viable manner.

Medical & Development

*Identify, evaluate and develop medicines specifically for Emerging Markets patients and health care stakeholders*
Pfizer’s China R&D Center: Integral to Global R&D

Strategic drivers: China market growth, competitive positioning, improved regulatory environment and commitment to international standards, strong talent pool, cost savings opportunities

One of the first and largest captive R&D centers by MNC

September, 2009
N = 350
Clinical Development Asia

Statistics
• 7/9 are PhDs
• 7/9 have an average of 6 years US experience
• Most of them lead projects

Enhanced Clinical Trial Design
Model-based drug development
Quantitative decision making

Clinical Sciences
Primary Care (Alzheimer’s Disease)
1st AD trial in China – Sponsored by PC BU
China Longitudinal Study to train Chinese sites

Clinical Pharmacology & Pharmacometrics
Academic collaborations in China & Korea
• Peking University-Pfizer
Pharmacometrics Education Center
• Pfizer Modeling & Simulation
Education Center Korea
Challenges in Drug Development for Pharma
• Regulatory Agencies focused on developing capability to conduct science-based reviews of NDAs

• All Agencies are gaining experience, degree of sophistication has improved greatly over the past few years

• Many countries are updating their drug laws and issuing guidelines in accordance with the rapid development of their Regulatory Agencies (although change in law can lag behind)

• Greater connectivity between Regulatory Agencies within Asia and with FDA/EMEA/TGA
  • Some agencies make use of preferred reference countries (e.g. Taiwan, Hong Kong, Singapore)
  • ASEAN countries moving towards mutual recognition of GMP inspection

• Trend towards acceptance of bridging strategies (ICH E5)
Regulatory Environment in Asia: Challenges

- No harmonized approach as found in EU – great diversity between Agencies
  - ASEAN harmonization efforts are at very early stage
- Level of expertise varies between regulatory Agencies:
  - few Agencies able to conduct full review
  - most rely on CPP
- Requirements have become more stringent in recent years
- Common issue with all Agencies is lack of manpower, none approach the level of staffing found within the EMEA or US FDA
- Presence of local Company expertise important since many regulations and guidelines not translated and nuances sometimes lost when translation exists

Increasing diversity of patients participating in global clinical trials leading to US FDA & EMEA concerns about relevance of foreign data to their own populations
Operational Challenges are Global

- Increased competition
- More studies competing for investigators/patients
- Increasingly complex studies
- Higher costs
- Pressure to reduce study start up times
- Subject recruitment challenging

Quality, Speed and Cost reduction are strategic imperatives
Speed, Quality, Cost in Asia: Proven Performance

**Speed**

Recruitment Rate
Number of New Patients Per 100 Sites Per Week

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<th>Global Average</th>
<th>Korea</th>
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**Quality**

Data Clarification Form Rate
% DCFs (Errors Per 100 pages)

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**Cost**

Investigator Non-Performance

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http://CMV.Pfizer.Com for Quality metric (data extracted in 2007)
Source: Clinical Trial Magnifier Vol. 2:4 Apr 2009
www.ClinicalTrialMagnifier.com

Figure 7. Number of US FDA Data Audit site inspections between 1997 and 2008 by geographic region; the proportion of inspections classified as Official Action is also provided. Values from Table 4.
GCP Compliance: A Challenge?
• Potentially relevant differences in the medical environment between and within countries
  
  • Standard of care
    – Background therapy
    – Referral route (i.e. pathway to inclusion in clinical trial)
  
  • Performance of endpoints
    – Cultural influence on patient reported outcomes
    – Subjective endpoints, physician assessments
  
  • Differences in placebo response, dropouts, motivation for patients to enroll in study

• The inclusion of patients in clinical trials should reflect as far as possible the patients who will ultimately take the medicine
Alzheimer’s Disease in China
A Case Study
Alzheimer’s Disease: Medical Need in Asia

- Strong & growing medical need across Asia
- Appropriate & necessary to include Asian patients in global trials
- Do we know enough to do this successfully?

**Total Prevalence: China, India, and Other Regions, 2005–2050**

Source: Dementia In The Asia Pacific Region: The Epidemic Is Here. Asia Pacific Members of Alzheimer’s Disease International. September 2006
Alzheimer’s Disease in China: What is Known?

• Poor disease awareness
  • Mild Cognitive Impairment does not present to doctors; considered normal aging by family
  • Alzheimer’s Disease usually presents as moderate to severe

• Low proportion (<30%) of patients diagnosed and treated (50-70%)

• Patients may be treated with herbal medicines

• Government-funded cross-sectional and longitudinal community-based and hospital-based MCI study (“ChADNI”)

• Pfizer funded cross-sectional hospital-based clinical survey of dementia care in China in progress:
  • dementia subtypes
  • co-morbidities
  • diagnosis and treatment rates
Alzheimer’s Disease in China: What Do We Need to Know?

• Is progression over time on cognitive (e.g. ADAS-cog) and functional measures (e.g. DAD) similar to western cohorts?
• Prevalence of APOE 4 allele in clinical trial population?
• What is the incidence of concomitant vascular disease over time?
• Do caregivers perceive symptoms differently than ones in US/Europe?
• What aspects of NPI are most affected in Chinese AD subjects?
• What is perceived disease burden in China?
• Do changes in biomarkers and brain volumetrics correlate with long-term cognitive, global and functional outcomes?
• How does background therapy differ in a clinical trial cohort?

How can we fill this knowledge gap?
A Longitudinal Study Can Fill Knowledge Gaps

• A 12-18 months duration in subjects with mild to moderate AD residing in urban areas in China

• A quantitative, longitudinal assessment of changes in relevant clinical and biologic markers as well as impact of disease on measures of quality of life in Chinese vs. Western

• Bridge gap in Pfizer’s portfolio by engaging investigators for early phase studies

• Enabler and methodology study to develop Chinese sites for contribution to AD studies for global registration

• Integrate data from China study into disease model based on Western data
Summary & Conclusion

The geographic location for drug development should reflect the patients that will ultimately be treated with new medicines.

Drug development in emerging markets brings similar challenges as conventional regions.

Potential for valuable and effective partnerships between Pharma, Regulatory Agencies & medical community as medical & regulatory environment is rapidly evolving.