



# Emerging Markets as Opportunities, Rather than Threats

DCAT Week

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March 12, 2008

## Backdrop

- Growth Expectations for 2008
  - US and EU5: 4-5%
  - Japan: 1-2%
  - BRIC: 12-13%
- Brand pharma
  - Innovation slump
  - Blockbusters losing patent protection
- Generics
  - Increasing competition, especially from India
  - Low cost API coming from India, China
  - Margin pressures in U.S., UK, Germany
  - Drop in small molecule opportunities post-2011

## Agenda

- Players
  - Big Pharma
  - Generics based in regulated markets
  - API manufacturers based in regulated markets
- Areas of opportunity:
  - Dose and API sales
  - R&D and Manufacturing base



## Market for Dose: India



- Big Pharma
  - Has been there for years: J&J, Wyeth, Pfizer, AZ, Glaxo, Lilly, Abbott, others
- Generics
  - Baxter: Leader in IV solutions market in India
  - Mylan: Matrix acquisition motivated only by access to API?
  - Teva: Perennial rumors about a major Indian acquisition

## Market for Dose: India

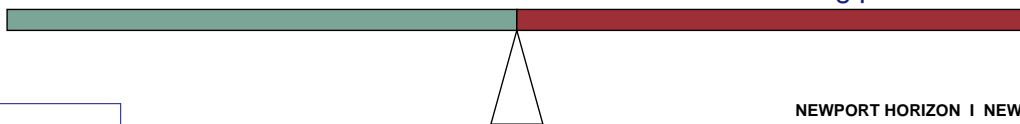


- Pros

- Double-digit pharma market growth
- Economic boom
- Growing middle-class
- Increasing prevalence of Western diseases
- 2005 product patents

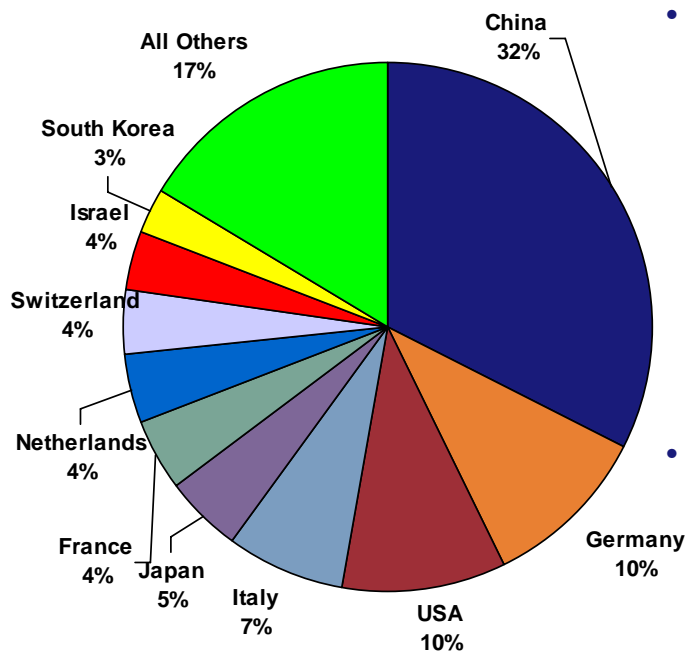
- Cons

- Challenges to product patents
  - Novartis's Glivec
  - Roche's Tarceva
- Potential for compulsory licensing
- Many people still lack access to pharmaceuticals
- Poor infrastructure
- Large number of backward integrated local generic drug companies
- Dose imports from China
- Low prices
- Restrictive import duty on finished dose products
- Need marketing presence



## Markets for API: India

~1200 Indian Import Registrations filed since Feb 2003



- EU/US based companies with most IIRs

- DSM
- BASF
- Schering-Plough
- Sanofi
- Novartis
- Pfizer
- Bayer
- E.ON
- Glaxo

- Products with most Euro/US IIRs

- Amoxicillin
- Clavulanate Potassium
- Pancreatin
- Beta Carotene
- Lactulose

Source: Newport Horizon

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## Market for API: India

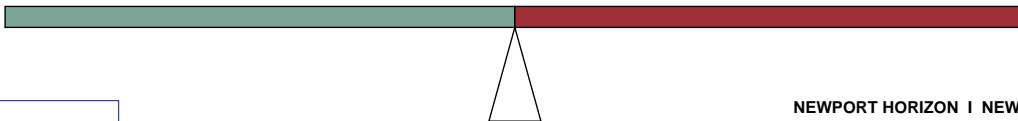


- Pros

- Not self-sufficient in all products
  - Fermentation
  - Steroids
  - Prostaglandins
  - Polypeptides
- Demand for Intermediates
- Costs rising in China and India
- Opportunities in high-quality API for export dose

- Cons

- Abundance of locally manufactured API
- Many local facilities FDA approved
- Extensive importing from China
- Local API manufacturers enjoy cost advantage
- Restrictive duty on API imports



## R&D and Manufacturing Base: India



- Big Pharma
  - Many have R&D and manufacturing sites in India: Novo Nordisk, Merck, Pfizer, others
- Generics
  - Sandoz: a number of units
  - Teva: small API/intermediates plant and R&D facility
  - Apotex: manufacturing and R&D facilities
  - Mylan: Matrix acquisition
- API Manufacturers
  - Trifarma: Alchymars ICM
  - Albany Molecular: FineKem, Ariane Orgachem

## R&D and Manufacturing Base: India

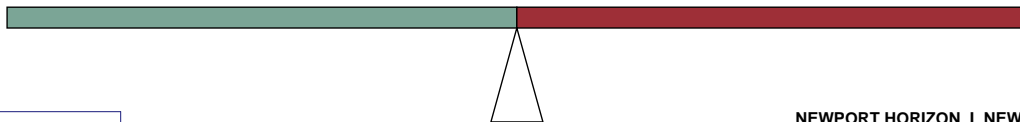


- Pros

- Scientific talent
- Significant cost saving opportunities
- Proven abilities in IT arena
- Product patents introduced in 2005
- 100% Foreign Direct Investment permitted
- Huge treatment-naïve patient population
- A number of sites with experience with submitting data to FDA
- Large English-speaking population

- Cons

- Costs increasing
- IP Issues
- Long-distance management
- Infrastructure
- FDA-approval doesn't necessarily mean consistent quality and cGMP compliance



## Markets for Dose: China



- Big Pharma
  - Has been there for years: Abbott, AstraZeneca, Boehringer Ingelheim, Eli Lilly, J&J, Novartis, others
- Generics
  - Baxter
  - Actavis: Actavis (Foshan) Pharmaceutical Co., Ltd.
  - Stada: Health Vision Enterprise, Stada Pharmaceuticals (Beijing)
  - Sandoz: Guangdong Sandoz Pharmaceutical Company
  - Teva: Tianjin Hualida Biotechnology Pharmaceutical (Sicor), Kunming Baker Norton (Ivax)

## Markets for Dose: China

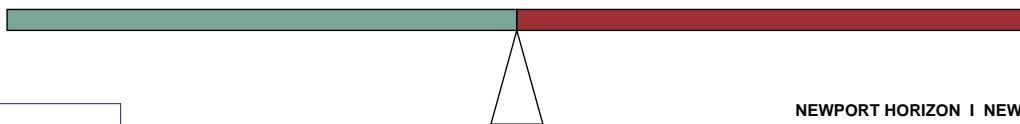


- Pros

- Expected to be the 5<sup>th</sup> largest pharma market by 2010
  - Growing middle class
  - Increasing life expectancy
- Increasing awareness of diseases and treatments
- Increasing prevalence of Western diseases
- Demand for cardiovascular, dermatological, oncology, pediatric drugs

- Cons

- Size of the country
- Fragmented market
- Many people still lack access to medicines
- Many government regulations that can slow down registration
- Competition from local players
- Must partner with local companies to get access to distribution channels
- Many Chinese companies active in individual provinces only
- Not all drugs currently sold in China
  - Generics may need to conduct clinical trials



## Markets for API: China

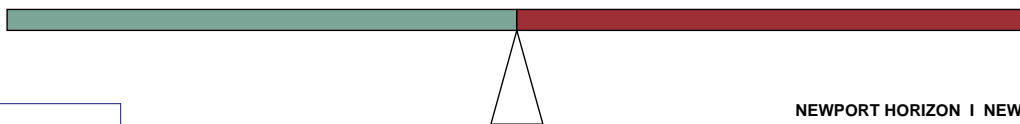


- Pros

- Rising costs in China
- Demand for difficult to manufacture APIs
  - “nibs”
- Demand for high-quality API from dedicated facilities
  - Newer cephalosporins

- Cons

- China has manpower, intellect and raw materials to manufacture most products locally
- Heavy focus on cost
- Importing from low-cost countries
- High-value of Euro



## R&D and Manufacturing Base: China



- Big Pharma
  - AstraZeneca, Novo Nordisk, Glaxo, BMS, Schering, Novartis, others
- Generics
  - Perrigo: Zibo Xinhua-Perrigo Pharmaceutical Company
  - Watson: R&D and manufacturing in Changzhou City
  - Sandoz: Guangdong Sandoz Pharmaceutical Company
  - Teva: Hualida Biotech
  - Baxter: at least four manufacturing facilities
- API Manufacturers
  - DSM: R&D, manufacturing
  - Esteve: Zhejiang Huayi Pharmaceutical
  - Lonza: R&D, manufacturing
  - Hovione: Zhejiang Hisyn

## R&D and Manufacturing Base: China

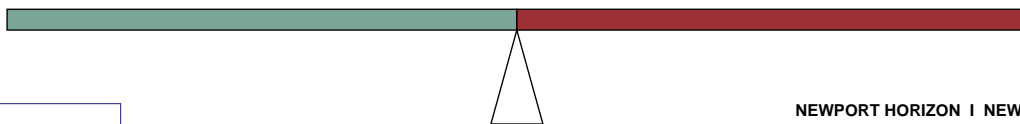


- Pros

- Talented pool of scientists, engineers
- Lower cost base
- Base for selling into other emerging markets
- Improving intellectual property protection
- Infrastructure
- Government support for R&D
- Large treatment-naïve population

- Cons

- Increasing prices
- Need for handholding and close monitoring
- FDA-approval doesn't necessarily mean consistent quality
- Risk of technology theft
- Environmental issues
- Language barriers



## Markets for Dose: Russia



- Big Pharma/Small Innovators
  - Roche, Sanofi-Aventis, Novartis, Nycomed, Pfizer, Menarini, Servier
- Generics
  - Lek, Gedeon, Krka – for decades
  - Stada, Pliva, Polpharma, Actavis

## Markets for Dose: Russia

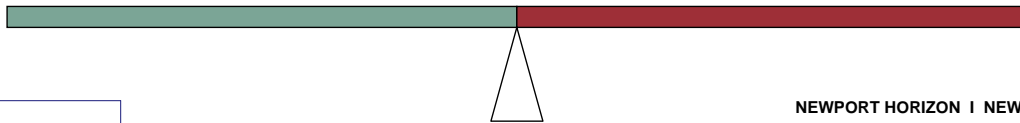


- Pros

- Growing middle class
- Demand for treatments for chronic diseases
  - No alternative therapies
- Obligatory health insurance
- Few local dose companies with cGMP experience
- Market dominated by imports

- Cons

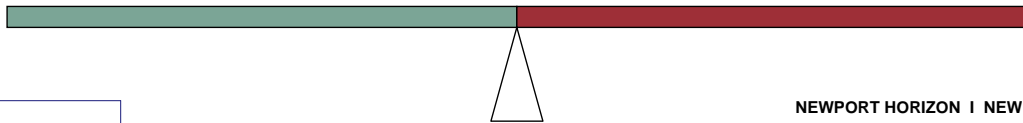
- Size of the country
- Poor infrastructure
- Fragmented distribution network
- IP enforcement
- Counterfeiting
- Controlled pricing
- Gov't debt to pharma cos
- Red tape
- Protectionist measures by government



## Markets for API: Russia



- Pros
  - Almost all API is imported
    - Little local production
    - Little local expertise outside of supplements
    - Local products w/ inconsistent quality
  - Large number of local dose companies
- Cons
  - A lot of the API is coming from India, China
  - Many local dose companies buy from offshore distributors
    - Suspect quality
  - Red tape



## R&D and Manufacturing Base: Russia



- Innovators:
  - Servier: dose plant near Moscow
  - Nycomed, Glaxo, Pfizer?
  
- Generics:
  - Stada: Nizhpharm, Makiz group (Makiz, Skopinpharm and Biodyne Pharmaceuticals)
  - Actavis: ZiO Zdorovje
  - Krka: Production facility in near Moscow
  - Polpharma/Gedeon: Akrihin

## R&D and Manufacturing Base: Russia

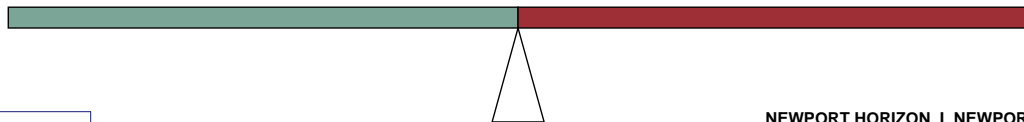


- Pros

- Low-cost production
- Platform for launching into CIS, E Europe
- Biotech and immunology experience
- Large clinical trial population
- Physicians eager to participate in trials
- Low cost of clinical trials

- Cons

- Erosion of formerly strong scientific base
- Poor enforcement of IP rights
- Counterfeiting
- Limited number of sites with GMP experience
- Red tape
- Economic and political risks
- Language barriers



## Markets for Dose: Brazil



- Big Pharma
  - Abbott, Boehringer Ingelheim, BMS, Pfizer, others
- Generics
  - Sandoz: only foreign generic co in top five
  - Apotex: exiting the Brazilian market
  - Teva: future plans?

## Markets for Dose: Brazil

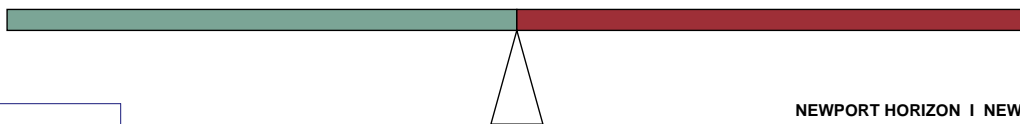


- Pros

- Largest population in Latin America
- Rapid market growth
  - Ageing population
- Gov't efforts to improve health care
- Gov't efforts to increase generics' uptake
- Opportunities with high-value specialty products

- Cons

- Price controls
- Frequent, abrupt changes of rules
- Lack of transparency
- Views toward IP
  - Efavirenz CL
- Generic market highly concentrated
  - Top four players: 80%
  - Domestic players dominate
  - Fierce competition
  - Need local manufacturing to be viable



## Markets for API: Brazil

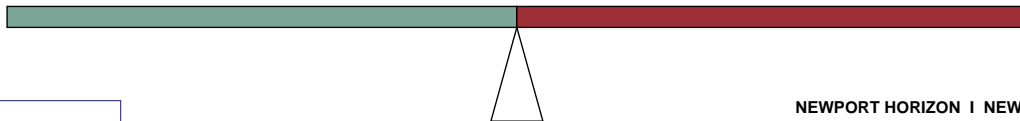


- Pros

- Most of API is imported
- Low import taxes
- Dose companies becoming more quality minded
- Regulatory environment becoming tougher
- Dose exports into neighboring countries
- Opportunities in
  - High-quality hormones
  - Controlled substances

- Cons

- Currently most API imports from India and China
- Still heavy focus on cost rather than quality
- Strong Euro



## R&D and Manufacturing Base: Brazil



- Big Pharma
  - Manufacturing base: Novartis, Roche, GSK, Janssen, Eli Lilly, Abbott
  - Ongoing clinical trials: BMS, Pfizer, Roche
- Generics
  - Sandoz: upgrading its manufacturing plant in Sao Paulo
  - Apotex: looking to sell the plant in Sao Paulo
- API Manufacturers
  - Italfarmaco
  - ACS Dobfar
  - DSM

## R&D and Manufacturing Base: Brazil

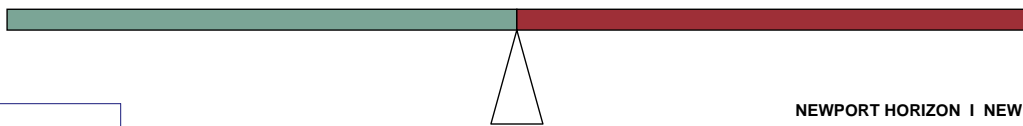


- Pros

- Biotech legislation
- Biodiversity and phytotherapeutics
- Platform for exporting into rest of Latin America
- Large treatment-naïve population
- Seasonal diseases 6-months out-of-synch with North America/Europe

- Cons

- Historically not strong in R&D
- Frequent, abrupt changes of rules
- Slow administrative processes
- Weak local API industry
- Language barrier



## Markets for Dose: Japan



- Big Pharma
  - Abbott, AstraZeneca, Boehringer Ingelheim, others
- Generics
  - Mylan: Merck Kgaa
  - Sandoz: Hexal
  - Hospira: agreement with Taiyo
  - Teva: aggressive plans for 2008

## Markets for Dose: Japan

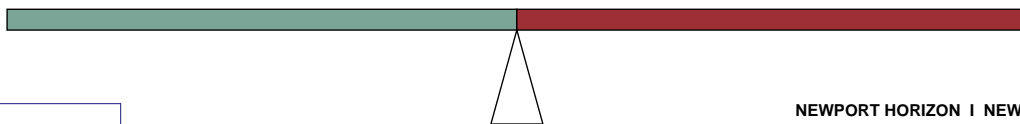


- Pros

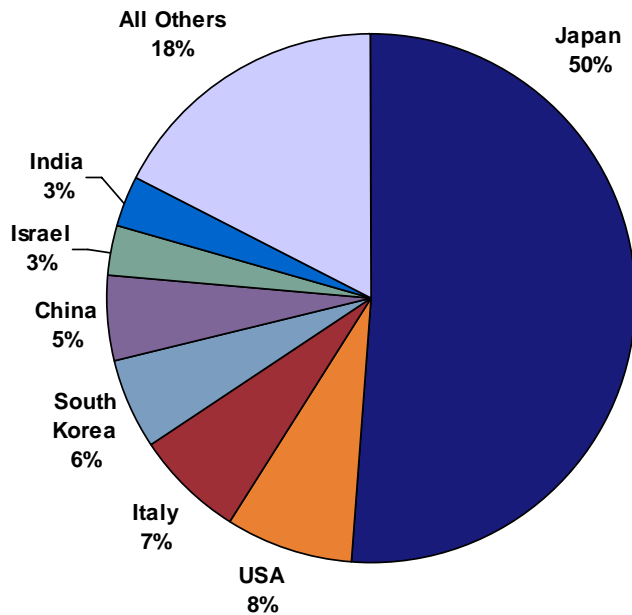
- World's second largest pharma market
- Ageing population
- All manufacturing can be done outside Japan
- Government aims to increase the market share of generics
  - Incentives
  - New Rx form
- Increasing use of OTC drugs

- Cons

- Slow approval process
- Price cuts/reduced reimbursement
- Slow overall growth of market
- Low image of generics
- Generics must provide every dosage/formulation
- Requirement for a nationwide distribution network
- Difficult for foreign companies to do it alone
- Underdeveloped framework for patent challenges



## Markets for API: Japan ~2000 JDMFs filed since Feb 2005



- EU/US based companies with most JDMFs

- Sanofi-Aventis
- Cambrex
- Schering-Plough
- Novartis
- DSM
- Pfizer
- BASF
- Merck & Co
- Erregierre
- FIS

- Products with most Euro/US JDMFs

- Heparin
- Mesalamine
- Terbinafine
- Omeprazole
- Itraconazole

Source: Newport Horizon

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## Markets for API: Japan

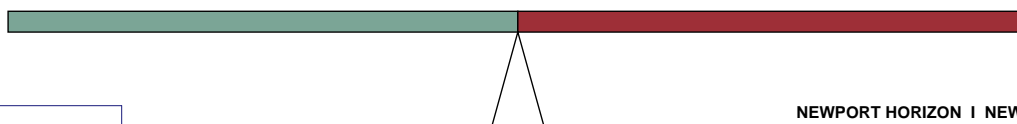


### • Pros

- Most dose companies do not make their own API
- Introduction of JDMFs
- New DMF and accreditation system discouraging certain players from less regulated markets
- Harmonization of rules
- CTD can be used as the basis for a DMF

### • Cons

- Different standards
- Relatively small volumes
- JDMF system still new
- Reliance on agents and well-established relationships
- Language barrier
- Many Japanese generics buying from India, China, South Korea
- Competition from Japanese fine chemical companies



## Main Opportunities for Regulated Market Players

	Pharma: Dose	Generics: Dose	API Sales	R&D	Manufacturing
India	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
China	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Russia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Brazil	<input type="checkbox"/>	<input type="checkbox"/> ?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> ?
Japan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## Thank you!

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