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INTELLECTUAL PROPERTY RIGHTS AND PHARMACEUTICAL PRODUCTS AND PROCEDURES

"Weathering the perfect storm"

by
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The perfect storm is brewing

- Patent expiries and loss of exclusivity – Exclusivity loss estimated to be around $11 Bn per annum for 2008 – 2011.
- Increasing payor pressure – Health care reforms in the US expected to put further pressure
- Generic competition from emerging markets
- Growing safety concerns - Increasing complexity and data requirements
- Brand Pharma has a perception problem – The Big Evil Pharma
- Increasing earnings pressure from the financial market

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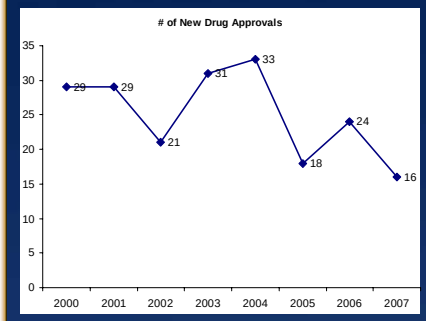
Productivity crisis



Pharma needs to be more productive and efficient to survive…

- Pharma's research output remains alarmingly low in spite of the slight uptick in 2008
- Patent expiries and loss of exclusivity – Exclusivity loss estimated to be around $11 Bn per annum for 2008 – 2011.
- Increasing payer pressure – Health care reforms
- Generic competition from emerging markets
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An unviable innovation model?

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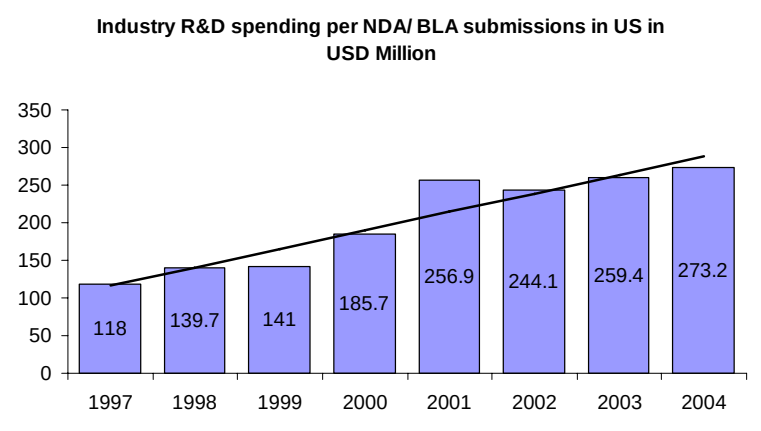

Base data source: **CMR International**

An unviable innovation model?

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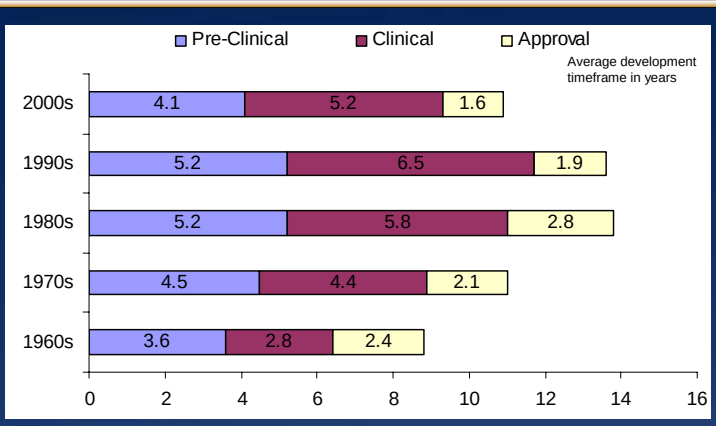
In spite of Industry's best efforts, Cumulative success rates are still low

	Pre-Clinical	Phase I	Phase II	Phase III/ File	Launch
1995 - 2000	8	6	3	2	1
		75%	37.5%	25%	12.5%
2000 - 2003	13	9	5	2	1
		68.23%	38.46%	15.38%	7.69%

With increasing payor pressures and shorter exclusivity periods, Pharma innovation is becoming unattractive to investors

Base data source: **Bain Consulting**

An unviable innovation model?



… In spite of the considerable improvement in the early 2000s, the average development cycle continues to cross a decade…

Base data source: **Tufts Impact Report**

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Need for newer solutions

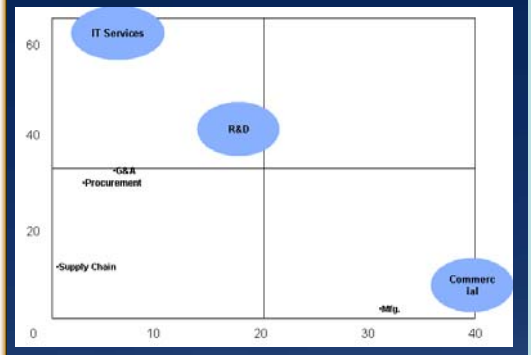
To reduce average drug development costs…

	.. By 100 Million	… By 200 Million
Reduce timelines by	**18.90%**	**41.30%**
Improve success rates by	**25.2 – 25.6%**	**30.4 – 31.7%**
Cut out of pocket expenses by…	**29.80%**	**59.60%**

Development process needs to be smarter, shorter and cheaper to make investments in innovation attractive…

Base data source: **Tufts Analysis**

Opportunity to rationalize cost-base



Share of employment in Pharma

- •Pharma is in the midst of aggressive outsourcing/off-shoring to rationalize it's cost structure
- •By 2008, the global resourcing demand in Pharmaceutical industry was expected to touch 254,000 FTEs
- •IT Services and R&D expected to lead the way
- •BRIC countries and South Africa are expected to be among the biggest beneficiaries

The slowly, but steadily changing game

- **Traditional belt-tightening leads to diminishing returns after an early success period**
- **Pharma has a lot to learn from product development practices in other industries**
- **Gap between development in pure science/ technology and it's applications**
- **Use of technology to eliminate unviable candidates early on, to speed up the development process and to improve the overall efficiencies is becoming mainstream**

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Domestic Pharma also needs a robust research infrastructure to sustain

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- South Africa is an excellent case in point:
- Strong domestic economy: Strong GDP growth (CAGR 9.4%) with sound fundamentals
- Growing disease burden: High infectious diseases and non-communicable diseases burden
- Strong domestic demand:
  - SA Pharmaceutical industry is growing rapidly
  - The industry currently estimated around USD 3 Bn +
  - Expected to touch $5.4Bn in 2012 at CAGR of 11.8%
- High quality manufacturing base
- Business environment for the Pharmaceutical industry may be getting tougher
  - Administered pricing regulations
  - Competition from India/China
- **The domestic industry needs a robust research eco-system to bring new molecules to the market and to address Africa's growing disease burden**

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But MNC Pharma and CROs have been ambivalent

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- **Need patience, commitment and long-term view to see potential despite set-backs**
- **Sales: "Chicken or the Egg" – if you are not in Africa you are not Global**
- **Infrastructural and regulatory concerns**
- **Intellectual property protection related concerns**
- Need to build a stronger case for Global Research Dollars for Africa?
  - What is our business case
  - What is our agenda for building capabilities

But there are critical challenges for the Pharma Industry AND The local Regulatory Authorities

Critical challenges……..

- Regulations on the conduct of Clinical Trials in Africa
  - Vary from country to country
  - Non-existent in many African countries
- Intellectual property protection
  - Finding the right balance between IP and public health needs
  - Addressing the concerns of the IP owner
  - Piracy and counterfeit drugs
- Regulatory approval delays
  - Lack of resources and infrastructure to review protocols
  - Lack of experienced talent
- Informed Consent / Possible ethical issues
  - Language of consent
  - Cultural impact on consent process
  - Impact of illiteracy on consent process
  - Consent in paediatric studies
- Investigator experience
  - Inexperienced Investigators and Site Staff could have a serious impact on the quality of data collected
- Infrastructure
  - Could be less than optimal at Investigator sites and third party contractors (e.g. local laboratories and couriers)

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Loss in FDI / Job opportunities

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- Global R & D spend $95 billion
- Global CRO outsourced $19 billion
- Local Pharma industry R2.88 billion
- Local CRO outsourced R1.73 billion
- Effect of approval period > 2 months by MCC for clinical trials
  - Loss of FDI: R286 million per annum
  - Job opportunities: 326

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Regulatory delays cost one S.A. company…

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- R109 million in Foreign Direct Investment
- R345 million in Nett New Business
- And 135 jobs

in 2008 !

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Show stoppers – Regulatory delays

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- Opportunity costs of Clinical Development delay – One day cycle time extension can result in lost revenues of USD 1 million or more *
- Any developmental delay impacting the Critical Path of the project are among biggest inhibitors of viability
- Emerging economies are constrained by the lack of regulatory bandwidth resulting in unacceptable approval delays
  - Current regulatory approval time frame in SA for Phase II/III study ranges upward of Nine months
- Such clog in the regulatory systems impact the ability of domestic pharma to bring in new products to the market
- A resource constrained regulatory infrastructure can also falter on the critical task of ensuring patient safety and appropriately mitigating risks
- Need to build a 21st century regulatory environment which can make us effective and competitive.

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Show stoppers – IP related concerns

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- Pharmaceutical industry looses billions of dollars globally every year to copies/counterfeits
- IP-related concerns of multinational Pharma – is confidentiality of data submitted for registration/CTA's a given?
- Drug supply and accountability, data submission requirements during development and registration
- Case for improving the domestic research output – Ensuring sufficient protections to make R&D viable

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Show stoppers – Health care and Drug Development are changing

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New science is changing healthcare

Structural Biology	Rational design of new medicines
Genetics, genomics and proteomics	Better targeting of medicines
Metabonomics	Better diagnosis and monitoring
Vaccines and immunomodulation	Prevention and monitoring of infectious diseases
Point of care diagnostics	Faster diagnosis and enhanced involvement of the patient
Bionics	Organ replacement and enhancement
Cell and tissue engineering	Regenerative medicine
Imaging	Better diagnosis and precision treatment
Micro-electronic devices	Sensing and monitoring; increased independence for individuals
Minimally invasive and robotic surgery	Enhanced precision and reduction in unwanted drama

Source: Sir Richard Sykes, Imperial College London

Emerging world of personalized medicine

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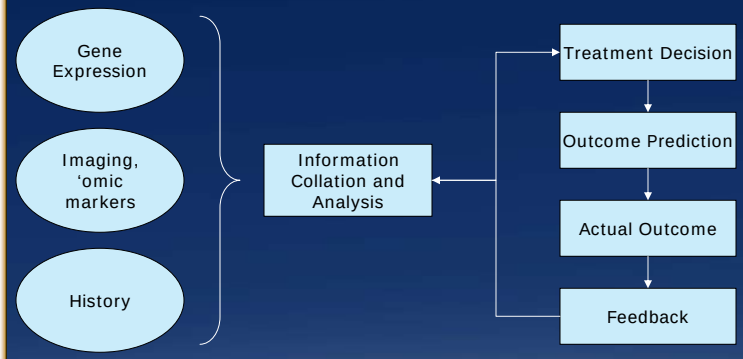
Granular understanding of disease models during development, Application of the accumulated knowledge from clinical development in Clinical Practices to deliver a better targeted, relevant cure…



..which will fundamentally change the commercial model of commercial drug development…

Need for newer models for development…

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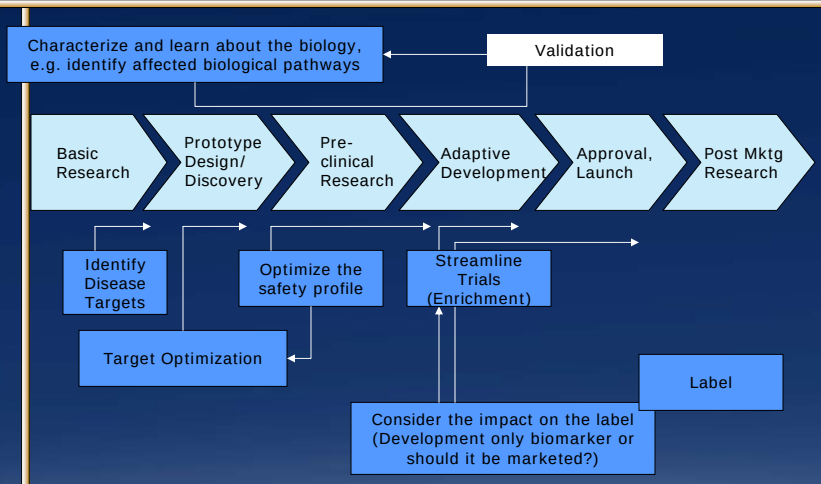

Source – Felix Frueh PhD, Harward Medical School

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Increasing use of Biomarkers

Technologies for Biomarker discovery and validation from genomics/ proteomics data are maturing

- **Possibility to replace a distant clinical end point with a more proximal surrogate end point**
- **Early elimination of unviable/ unsafe candidates**
- **Regulatory position on the acceptability of surrogate end points only evolving**
- **Biomarkers offer great value in optimal trail design, potentially bringing down the development costs**

The market for Biomarkers is expected grow from 0.5 Billion in 2003 to 2.8 Billion in 2008

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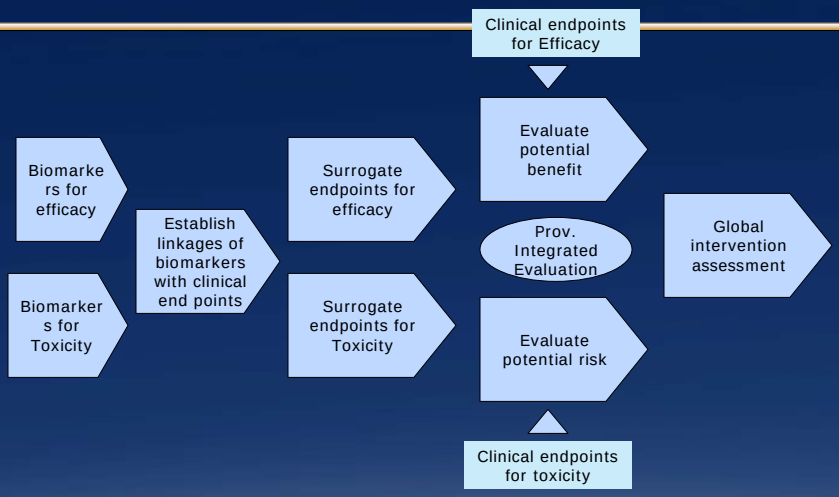
Biomarkers – A conceptual model



Providing the sponsors early exit options / conditional approvals in the accelerated path in select cases

* Reproduced from an FDA Paper

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…and potentially revolutionizing R&D

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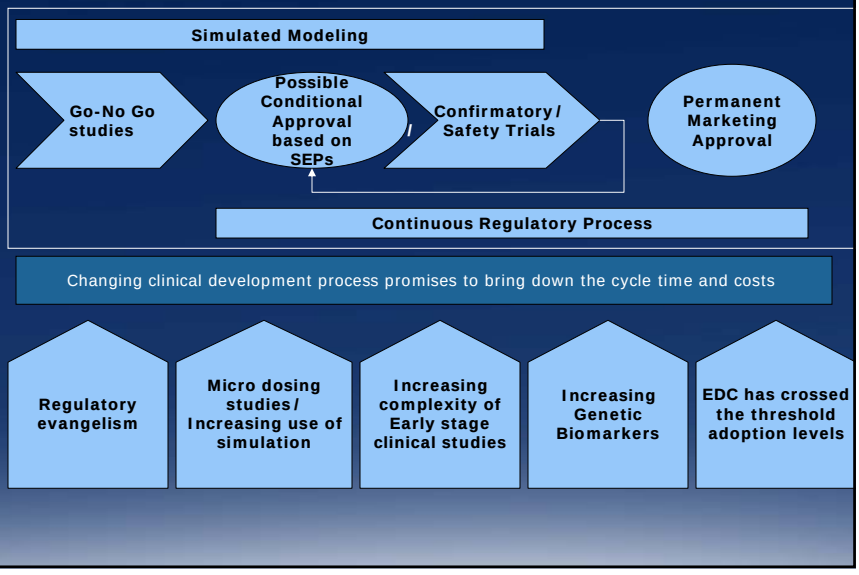

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Predictive bio-simulation

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Use of computer models to simulate the biological processes to weed out less promising drug candidates by understanding the likely impact of such candidates

- **Bio-simulation helps to interpret pre-clinical outputs in the context of human physiology**
- **Use of virtual patients**
- **Increased predictability of clinical outcomes**
- **Optimal design of trial protocols**
- **Use in identification appropriate surrogate end-points and bio-markers**

"if Boeing developed an Aircraft the way Pharmaceutical industry develops drugs, they would develop 10 very different aircrafts, fly them, and the one that stayed in the air would be the one they would sell" – Tom Paterson, CEO, Entelos

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Predictive bio-simulation

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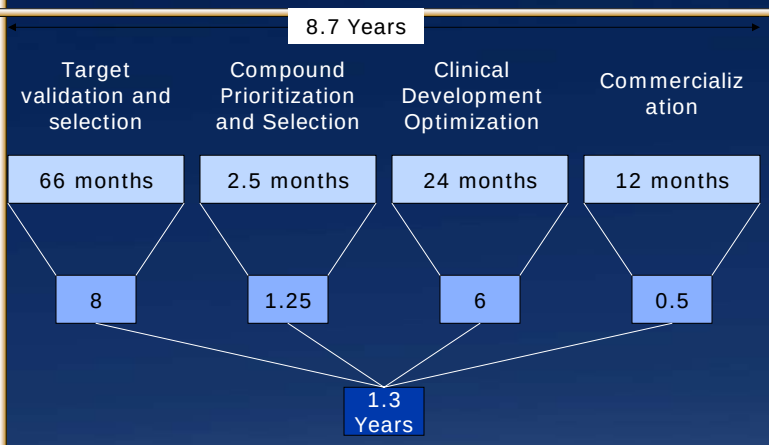

Illustrative time savings reported by an Entelos study, conducted along with the industry

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Predictive bio-simulation

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- **Early leaders gain visibility**
  - **Gene Network Sciences**
  - **Entelos**
  - **Pharsight**
  - **Rosetta**
- **Most frontline Pharma companies extensively use bio-simulation techniques (Pfizer, Roche, J&J, Novartis, to name a few)**
- **Mainstream CROs like PPD, Charles River, MDS, etc active in the Biosimulation space through partnerships or strategic investments**

Study designs – Further possibilities

FDA identified the following streamlining options in its follow-up to the Critical Path document:

- Non-inferiority trials
- Enrichment designs
- Adaptive trail designs
- Best practices in handling missing data
- Analysis of multiple end points
- Measuring disease-related symptoms and patient-reported outcomes
- Dose response relationships in Onclogy

e-MR to further streamline processes

- Increased visibility of source documents and patient related data across the chain
- Further reducing the on-site CRA role in Source Document Verification
- Data Privacy related regulatory positions lack clarity
- Scale of eMR adoption will depend on the progress on universal healthcare initiatives
- Need for vendor consolidation and data standards
- Need for integration between eDC systems and eMR environments
- Medium to longer term possibility

Show stoppers – Scalability

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- Global quality, GCP compliant Clinical Research is relatively nascent in Africa, compared to western economies
- Lack of a large enough pool of experienced clinical development professionals
- Inability to trigger a reverse brain drain, which many emerging economies are experiencing
- Dwindling/moderate academic output, resulting in generally anemic talent pools
- War for talent and resulting high attrition making captive training returns unattractive
- Dearth of good quality, experienced investigators willing to participate in trials
- Commercial viability of investigator sites

Case for Public – Private partnership

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- Need for proactive Public – Private partnership to build capabilities and infrastructure
- A five point plan towards global competitiveness

Streamline the regulatory/IP framework	Rationalize the Regulatory/Intellectual property framework to offer faster approval timeframes, less bureaucratic hassles while ensuring subject safety.
Augment the regulatory infrastructure	Industry and Government to work together to bring in talent and augment infrastructure
Work with schools/universities	Industry to work with Schools and Universities to augment/tailor the curriculums to better shape students to meet the needs of the clinical research industry
Vocational bridge programs	Industry or private educational service providers to develop targeted bridging courses to address the skill gaps of the college output
Profitable research practices	Work with investigators to conceptualize and build successful research practices

Africa has the potential to be a clinical research powerhouse, But it requires a coordinated effort to build capabilities, streamline regulatory system and to be competitive globally…

It takes a village…

Q & A

Thank You