



EMORY

Bridging The Valley Of Death In Academic Drug Discovery

A NEW PARADIGM FOR 21ST CENTURY DRUG DISCOVERY

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UNIVERSITIES AND BIOTECH COMPANIES HAVE BECOME THE DISCOVERY ENGINES OF PHARMA

“Today...two-thirds of the roughly 3,000 drug compounds currently under development were engineered in biotech labs.... Just as important, they were created at half the average cost of those at pharmaceutical firms.”

The Wall Street Journal (November 29, 1995)

“We expect that in the future a major portion of our drug pipeline will come from collaborations with external partners.”

Jeffrey Kindler, CEO Pfizer

“Collaboration with others in industry, academia, government and non-governmental organisations and healthcare in general is fundamental to our strategic priorities of growing a diversified, global business and delivering more products of value.”

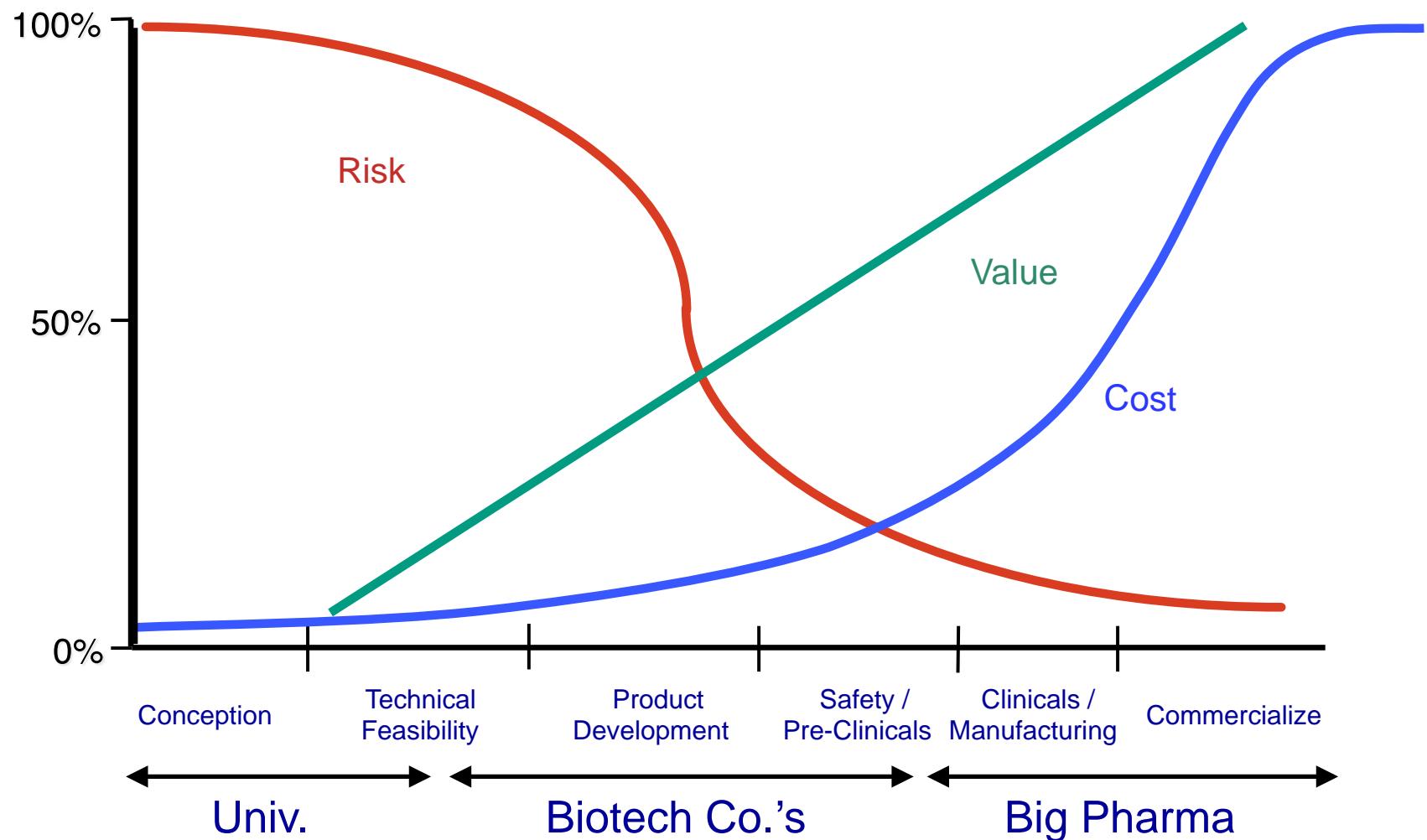
Glaxo SmithKline website



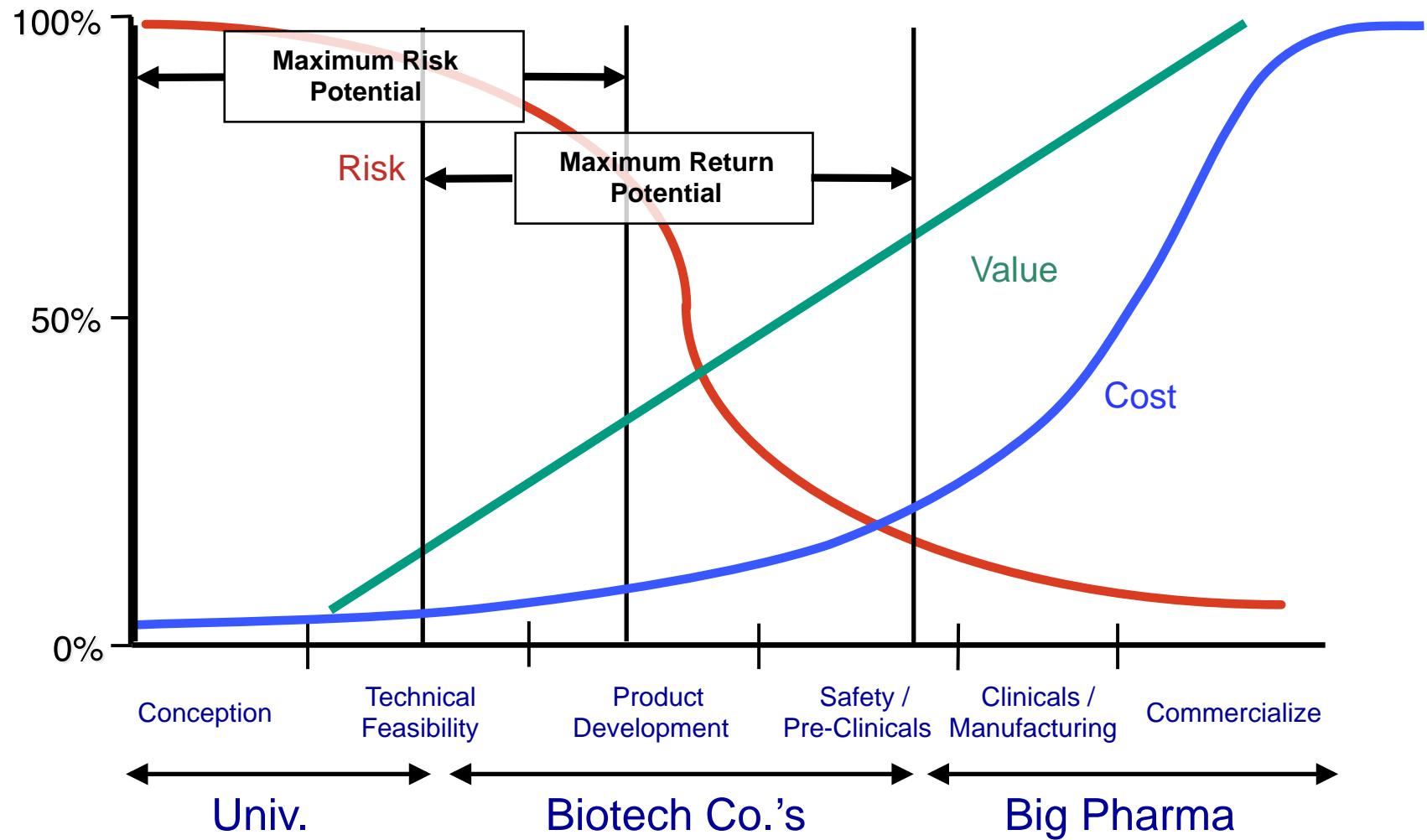
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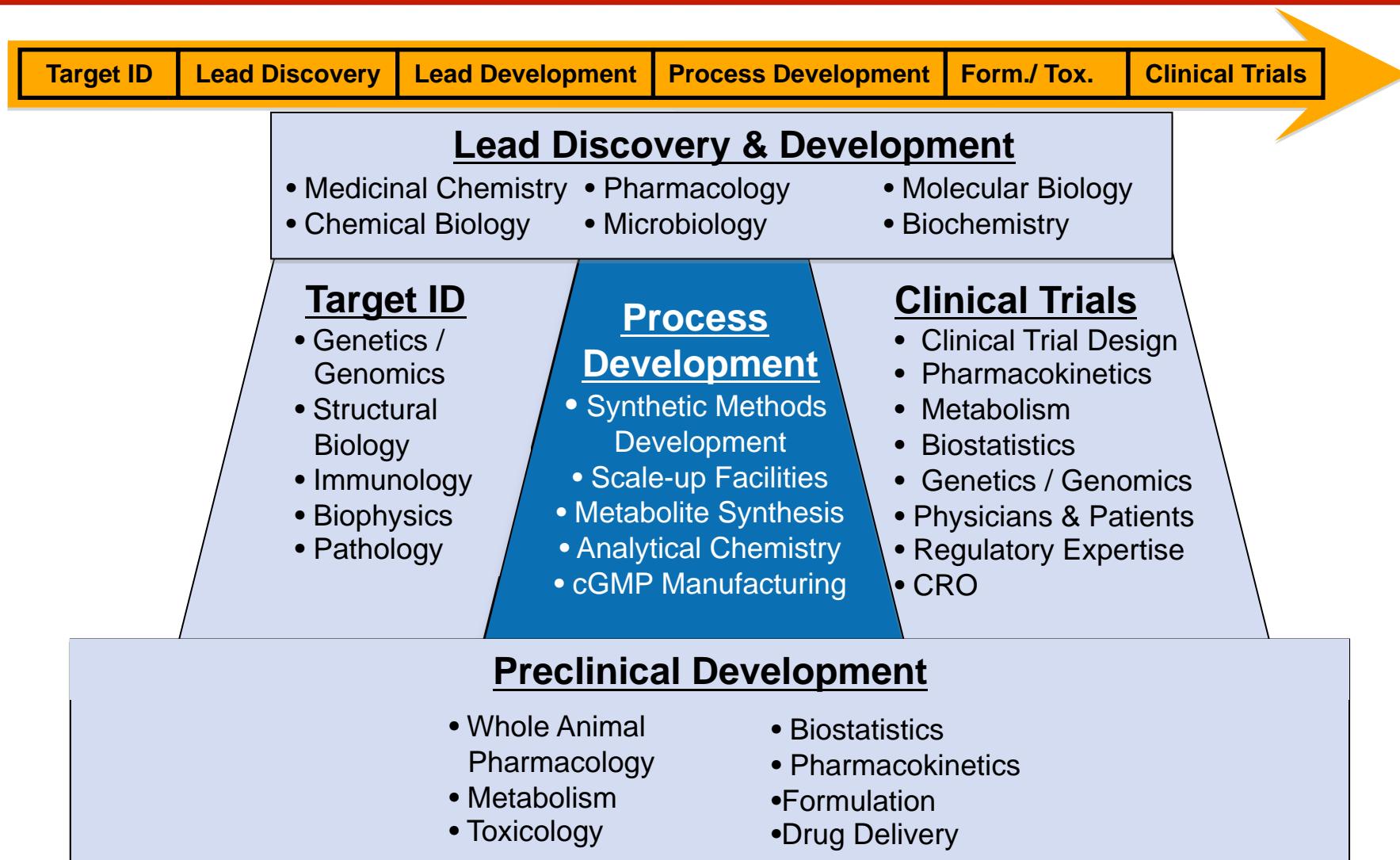
PHARMACO ECONOMICS 101



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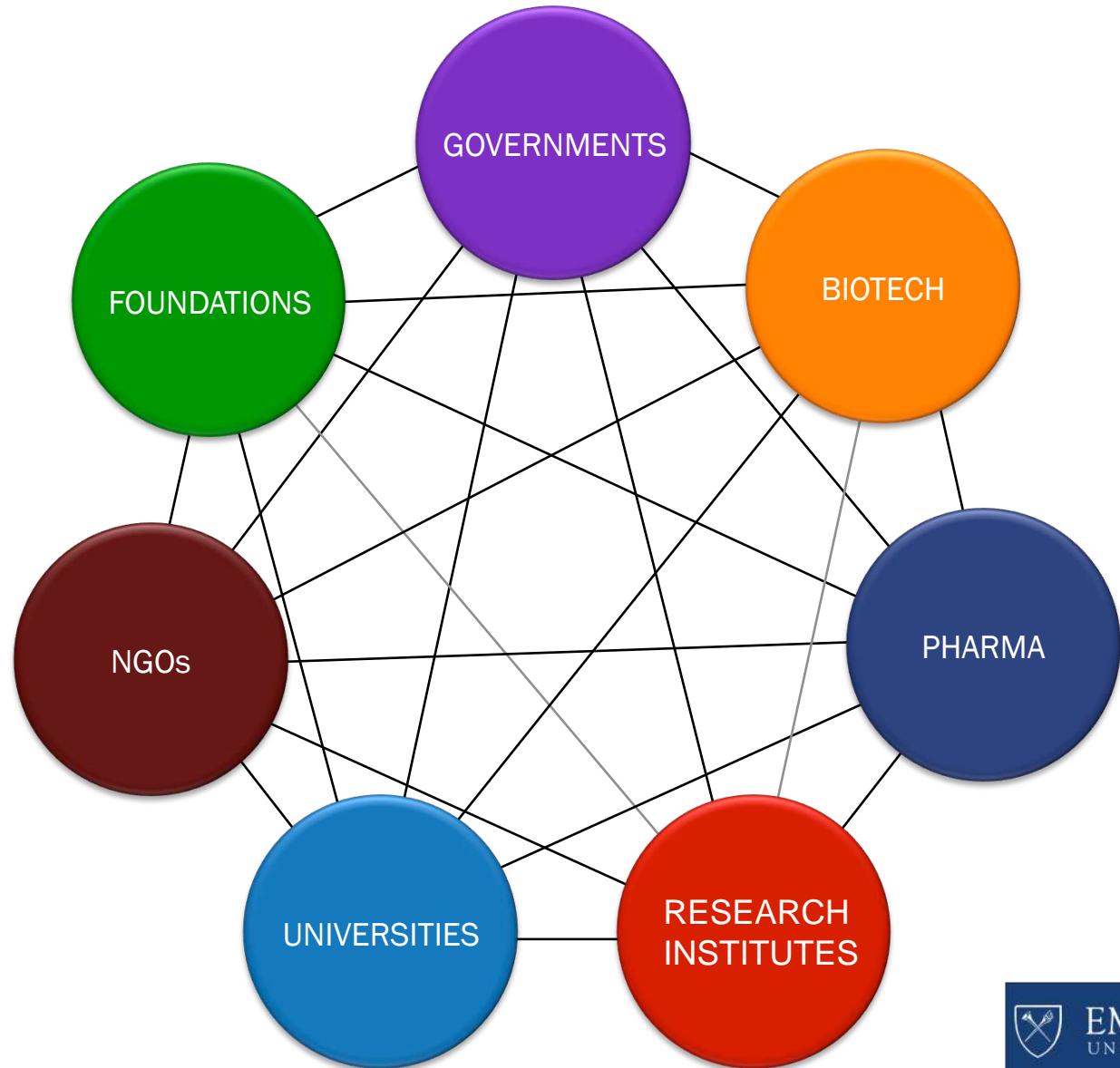
EXAMPLES OF DISCIPLINES REQUIRED FOR DRUG DEVELOPMENT



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GLOBAL NETWORKS WITH MANY PLAYERS



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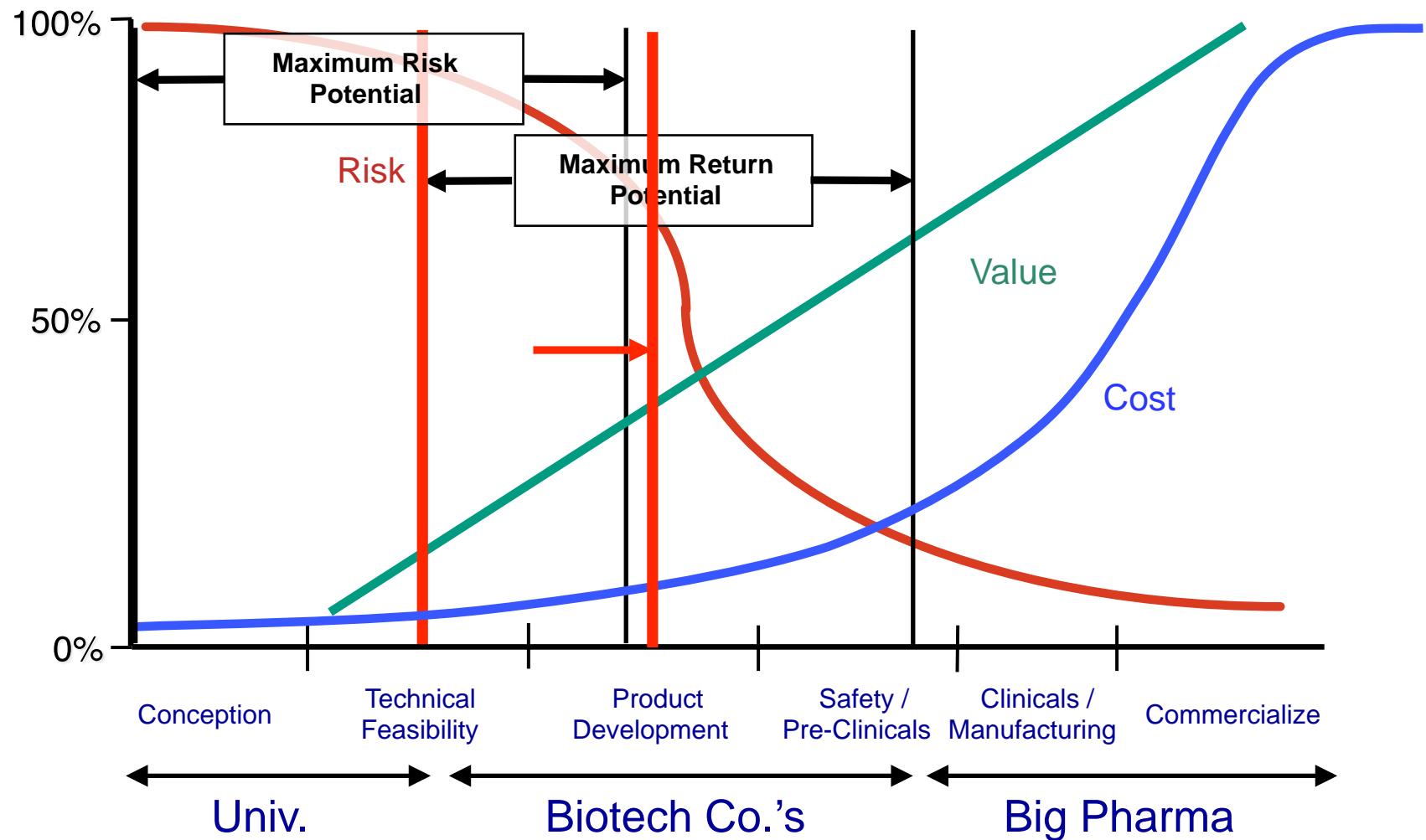
THE PROPER FUNCTION OF GOVERNMENT, NON-PROFITS AND PHILANTHROPIES

- Identify broad-based needs that can not be adequately addressed by the commercial sector.
- Develop strategic initiatives for catalyzing economic development in prioritized areas.
- Actively engage in human capital development:
 - Training scientists
 - Training entrepreneurs
- Develop infrastructure (a national informatics backbone, high tech instrumentation, professional expertise, etc.) with broad availability to the academic and commercial sectors.
- Develop partnerships that facilitate scientific exchanges across borders.
- Provide special incentives for startup companies.

BENEFITS OF UNIVERSITY-BASED DRUG RESEARCH

- Drug discovery research in academia provides an important complement to the discovery activities in Pharma.
- The emphasis by universities on basic research provides a natural platform to identify potential therapeutics.
- Research carried out in academia is not immediately dictated by the needs of the marketplace.

PHARMACO ECONOMICS 101

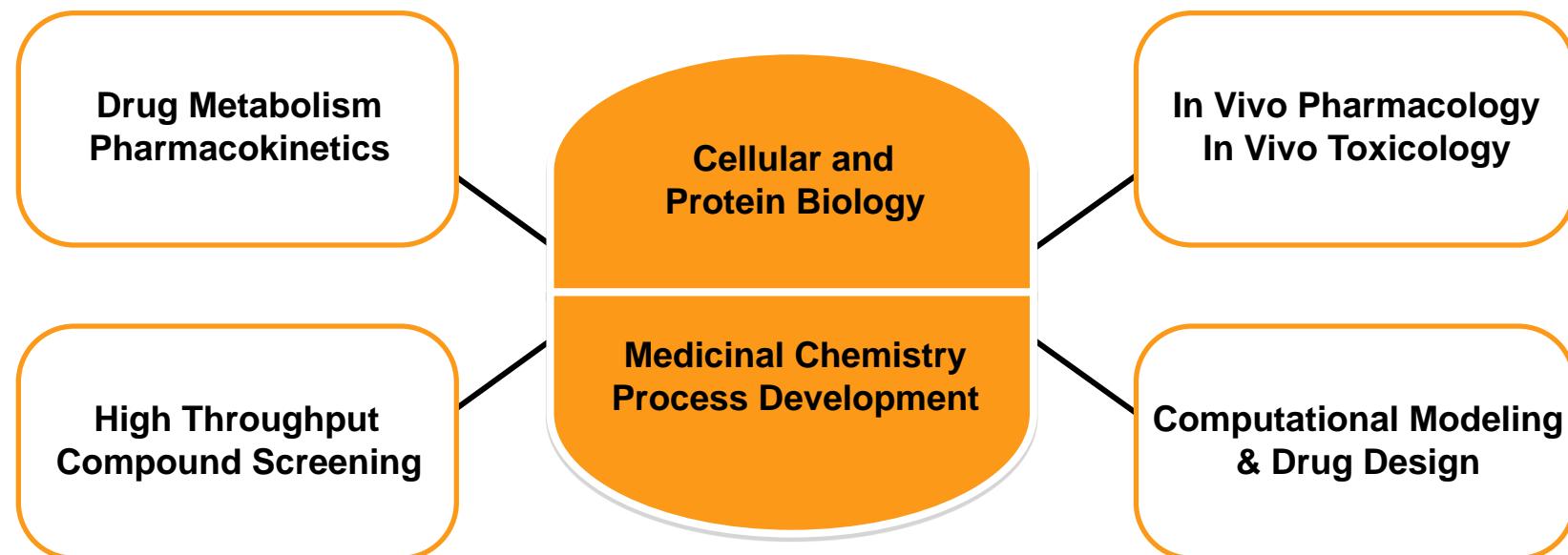


THE EMORY UNIVERSITY PRODUCT PIPELINE

Product Pipeline

PRODUCT PIPELINE: THERAPEUTICS								
Product	Licensee	Indication	Preclinical	Phase I	Phase II	Phase III	NDA	Market
3TC (Combivir®)	GlaxoSmithKline/Shire	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
3TC (Epivir®)	GlaxoSmithKline/Shire	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
3TC (Epivir-HBV®)	GlaxoSmithKline/Shire	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
3TC (Epzicom™)	GlaxoSmithKline/Shire	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
3TC (Trizivir®)	GlaxoSmithKline/Shire	HBV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
FTC (Atripla™)	Gilead Sciences, Inc.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
FTC (Emtriva®)	Gilead Sciences, Inc.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
FTC (Truvada®)	Gilead Sciences, Inc.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
AGI-1067	AtheroGenics, Inc.	Atherosclerosis	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
B-L-Fd4C (Elvucitabine)	Achillion Pharmaceutical	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
AGI-1096	AtheroGenics, Inc.	Rheumatoid Arthritis	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
DAPD (Amodoxovir)	RFS Pharma, LLC	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
DFC (Dexelvucitabine)	Pharmasset, Ltd.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
eeFTC (Racivir®)	Pharmasset, Ltd.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
LAP (Factor VIII)	Octagen Corporation	Hemophilia	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
CUR-770	Curry Pharmaceuticals	Psoriasis	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
DNA/MVA HIV Vaccine	GeoVax, Inc.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
Phenoxybenzamine	WellSpring Pharmaceutical	Graft Vasospasm	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
Glutathione Lozenges	GT-PLUS	Influenza	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
Histone Methyltransferase	Chroma Therapeutics	Cancer	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
LIP (Factor VIII)	Octagen Corporation	Hemophilia	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
LMP-1	Medtronic Sofamor Danek	Bone Disorders	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
Noscapine	Cougar Biotechnology, Inc.	Anti-Tumor Cancer	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■
2'-Fluoronucleosides	Pharmasset, Ltd.	HIV	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■	■■■■■

THE EMORY INSTITUTE FOR DRUG DISCOVERY



- A multidisciplinary environment staffed with experienced investigators
- State of the art bioanalytical instrumentation
- An array of computational design programs and hardware
- Fully equipped chemistry and biology labs
- Access to fully staffed rodent and non-human primate vivaria

PARTNERING WITH THE DEVELOPING WORLD

South Africa is an excellent example of the advantages that can emerge from partnering with **Developing World** nations.



- **Strong research science:**
 - Research universities and institutes
 - Government research councils
- **Unique biodiversity:**
 - Cape Floristic Region
 - National Botanical Garden
- **Traditional Knowledge Systems**

“Africa’s real compound GDP growth, about 5 percent annually between 2002 and 2009, was on par with Russia’s and significantly higher than those of developed countries..... 4.5 percent until 2015, which will boost consumer spending by more than 35 percent”

– McKinsey Quarterly, June 2010

EXAMPLES OF SOUTH AFRICA'S GROWING DRUG DISCOVERY INDUSTRY

- **iThemba Pharmaceuticals** - an emerging drug discovery company whose goal is to develop novel, small molecule therapeutics to address unmet medical needs in sub-Saharan Africa. iThemba recently merged with Arvir, a start-up biotechnology company focused on providing a strategic array of affordable antiretrovirals (ARVs) and microbicides (Capresa trial) through the establishment of local capacity for API (Active Pharmaceutical Ingredient) manufacturing.
- **ACRO** - a CRO which offers clinical research services to donor-funded organizations, non governmental organizations, research institutions, pharmaceutical companies, and government institutions.
- **Aspen** - Africa's largest pharmaceutical manufacturer and a major supplier of branded and generic pharmaceutical, healthcare and nutritional products to southern Africa and selected international markets.
- **Elevation** - a spin out biotech company from the University of the Witwatersrand and South African National Health Laboratory Service (NHLs) that is focused on the discovery and development of HIV attachment inhibitors.
- **Kapa** - founded to develop next-generation PCR reagents. Their molecular evolution technology platform is currently being used to optimize enzymes for DNA amplification, next-generation DNA sequencing, and molecular diagnostic applications.
- **Synexa** - a South African-based provider of specialized clinical trial laboratory services. This entity offers an extensive portfolio of non-routine laboratory analyses that provide a better understanding of the safety and efficacy profiles of clinical agents.

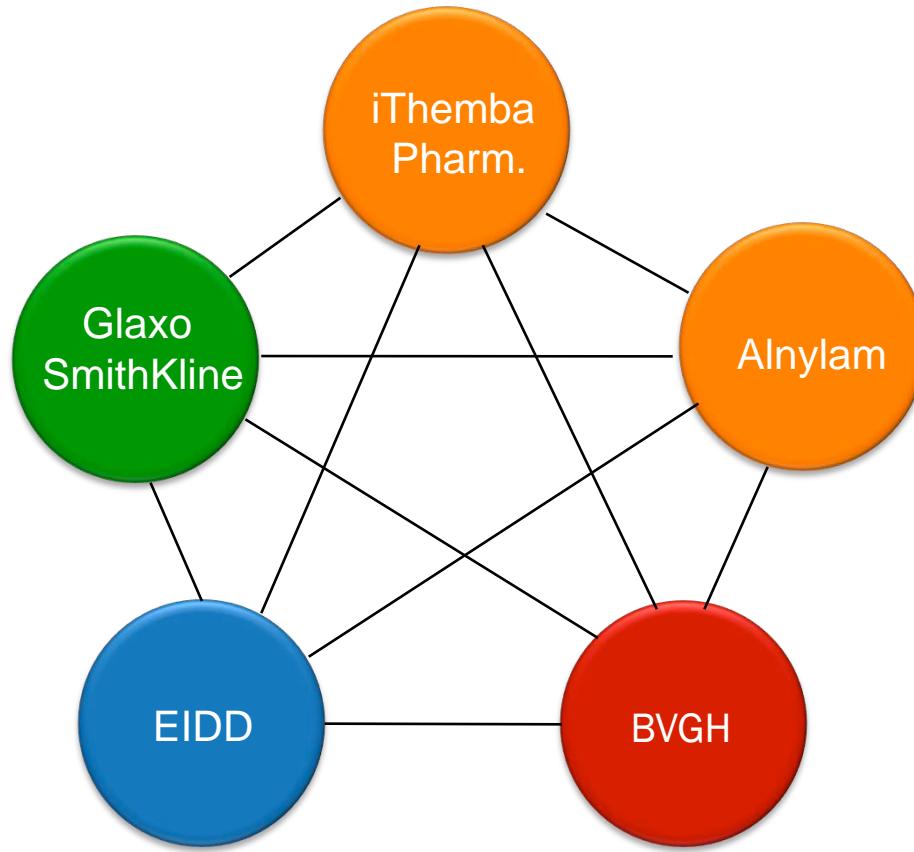
THE EMORY-SOUTH AFRICA DRUG DISCOVERY TRAINING PROGRAM

- Established in partnership with the government of South Africa (National Research Foundation).
- Yearlong postdoctoral and 6 month research advanced training programs in a number of disciplines including medicinal chemistry, biochemistry, computational chemistry, pharmacology, and bioinformatics. “Mini” sabbaticals are also available for more experienced individuals.
- Course in fundamentals of drug discovery (science, business, and law) and career development.
- 15 Scholars since 2008.
- Partners include SCYNEXIS, Inc. and GlaxoSmithKline, Inc. (2011).

THE SOUTH AFRICAN BIO PLAN COMPETITION

- Established in collaboration with the Innovation Fund (now a part of the Technology Innovation Agency) to help develop new life science companies in South Africa.
- 2 day workshop in patent law/licensing and entrepreneurship.
- Weeklong Executive Education provided by Goizueta Business School (Emory University) faculty.
- Mentorship from established biotechnology executives is provided to help assist the development of business plan.
- Business plan competition is judged by experienced Venture Capitalist from South Africa, USA, and Europe.
- Winners receives seed funding. All participants receive access to a powerful network of supportive entrepreneurs and scientists.

THE KNOWLEDGE POOL



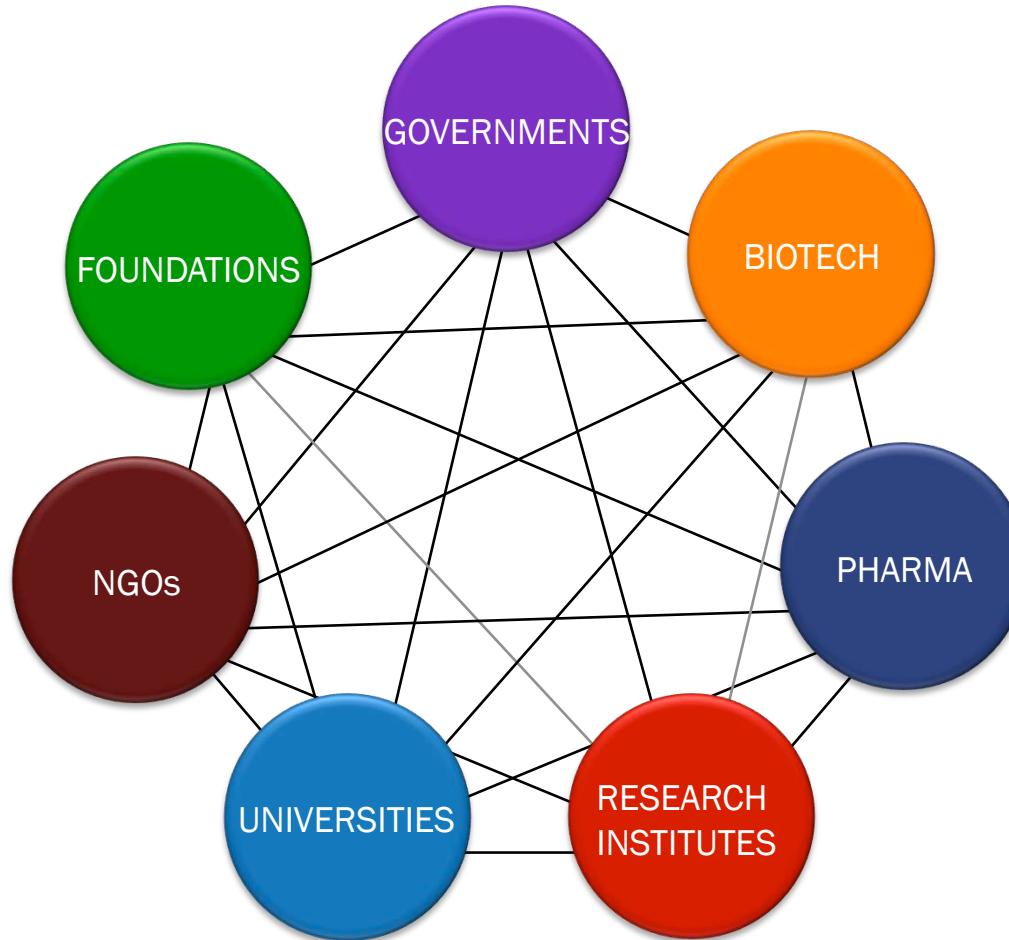
The collaboration is focused on inhibition of two enzymatic targets (isocitrate lyase and malate synthase) associated with latency stage of TB.

THE GSK - ITHEMBA - EIDD COLLABORATION

- GSK pays for flights from and to the country of origin.
- GSK pays for accommodations for visiting scientists.
- GSK pays scientists a competitive annual salary on a pro rata basis.
- Visiting scientists will spend 6 months in Tres Cantos, Spain, followed by 6 months in Moderfontaine, South Africa to complete the knowledge transfer process.

GLOBAL NETWORKS WITH MANY PLAYERS

**Develop
Capacity
Building
Partnerships**



**Bring New
Products and
Services to the
Marketplace**

**Become
Innovation
Boutiques**

THE ROLES OF AND OPPORTUNITIES FOR THE COMMERCIAL SECTOR (SMALL AND LARGE PHARMA)

Roles: Execute a focused business strategy for the efficient development of both individual and platform technologies.

Opportunities

SOUTH AFRICAN PHARMA OFFERS

- Low operating costs
- Minimal marketing overhead
- Conduit for global social investment
- Dual branding opportunities
- Expedient clinical development



PROFITABILITY POTENTIAL

Developing World:

- Good ROI
- Low margins / High volumes

Developed World:

- Excellent ROI
- Spectacular margins

Both Worlds

- Opportunity for reinvestment in R&D





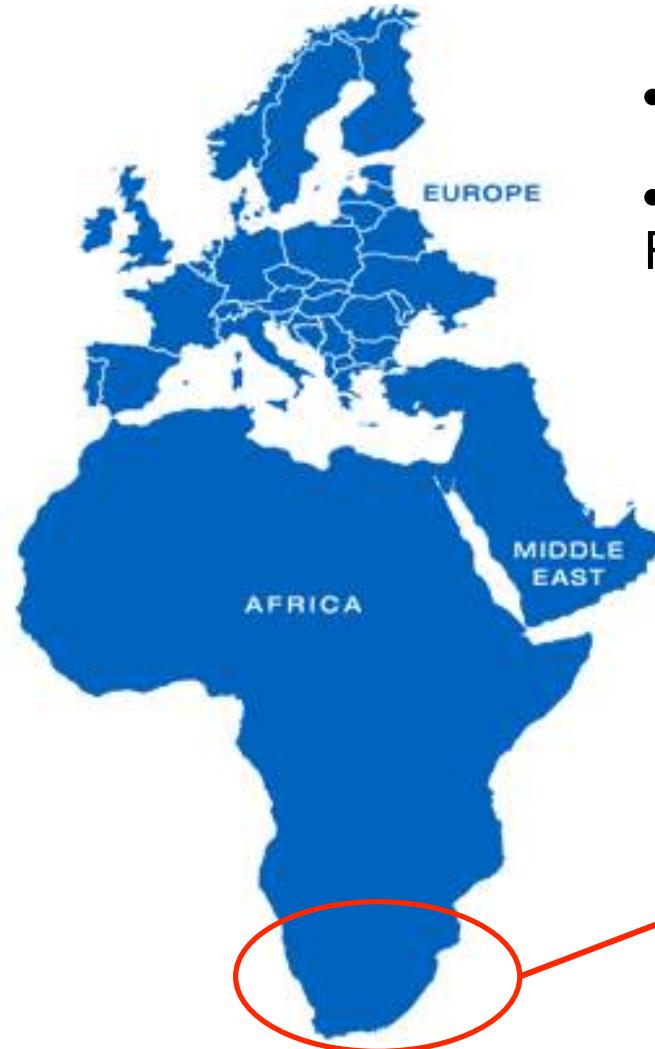
***Leader in Medicinal and Synthetic
Chemistry***

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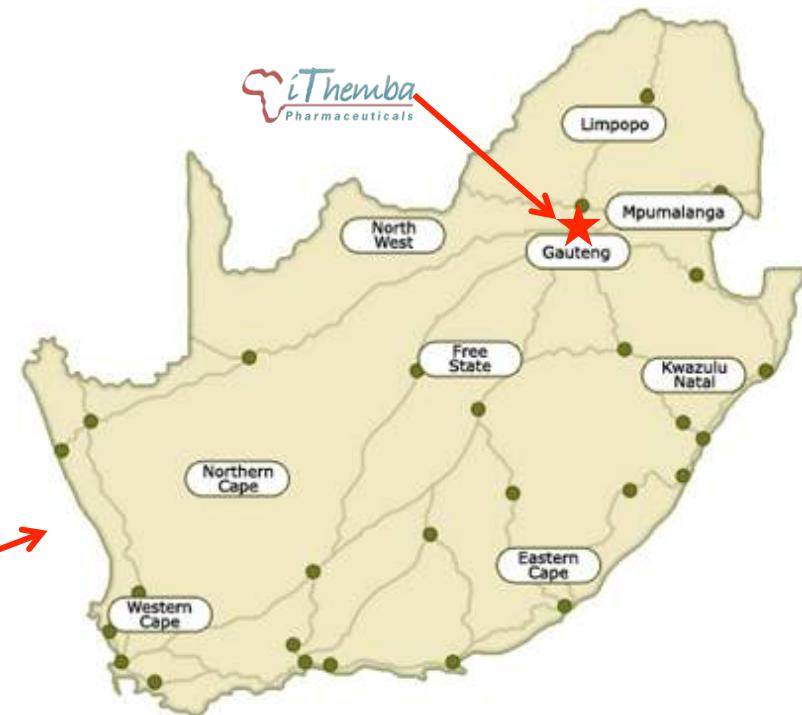
Overview of iThemba Pharmaceuticals

- Only small molecule Chemistry company in South Africa (and Africa)
 - Highest number of PhDs in Africa
- What do we provide?
- What is our expertise base?
- What do you gain by contracting with iThemba?
- Our track record

Location



- South Africa is GMT +2h
- Cape Town to iThemba = London to Rome



Board of Scientific Advisors

- Prof. Dennis Liotta (Emory University, Atlanta, USA; founding member and shareholder)
- Prof. James Bull (University of Cape Town, South Africa)
- Prof. Anthony G. M. Barrett (Imperial College, London, United Kingdom; founding member and shareholder)
- Prof. Erick Carreira (ETH, Zurich)
- Prof. Steven V. Ley (Cambridge University, England; founding member and shareholder)
- Dr. George R. Painter (Chimerix Inc., NC, USA)

A Few Facts

- Commenced operations: June 2008 with 4 staff
- Finance: R30M (\$4M) initial investment (government), a further R19M (\$2.5M) raised through collaborations
- Number of employees: 16 (10 PhDs)
- Facility: 800m² of laboratory space with state-of-the-art analytical and synthesis equipment (mg – 100g and array up to 20)
- Equipment: 400MHz NMR, Agilent LCMS and prep HPLC, Genevac, CEM discover 12 µW

Service Business

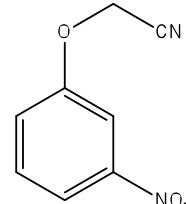
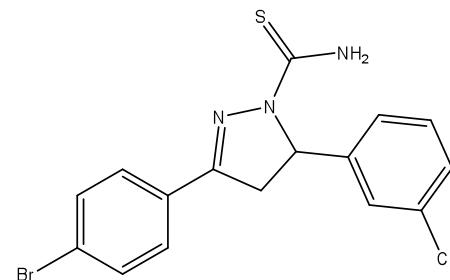
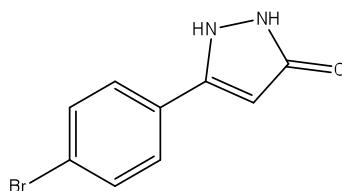
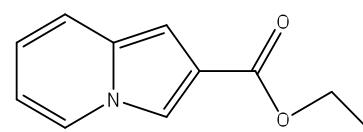
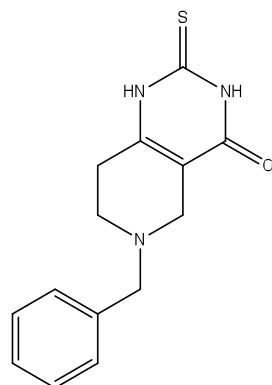
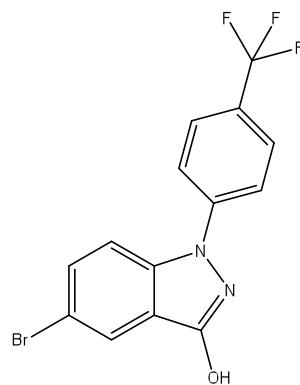
- Offer contract service (FTE or project-based)
 - synthetic organic chemistry
 - medicinal chemistry (via collaboration with AIBST)
- Top quality SAB
- Several international clients
 - repeat business
- Produce and sell novel chemical intermediates
- ‘Gold Standard’ Hit validation service

Service Business – In Vitro ADMET

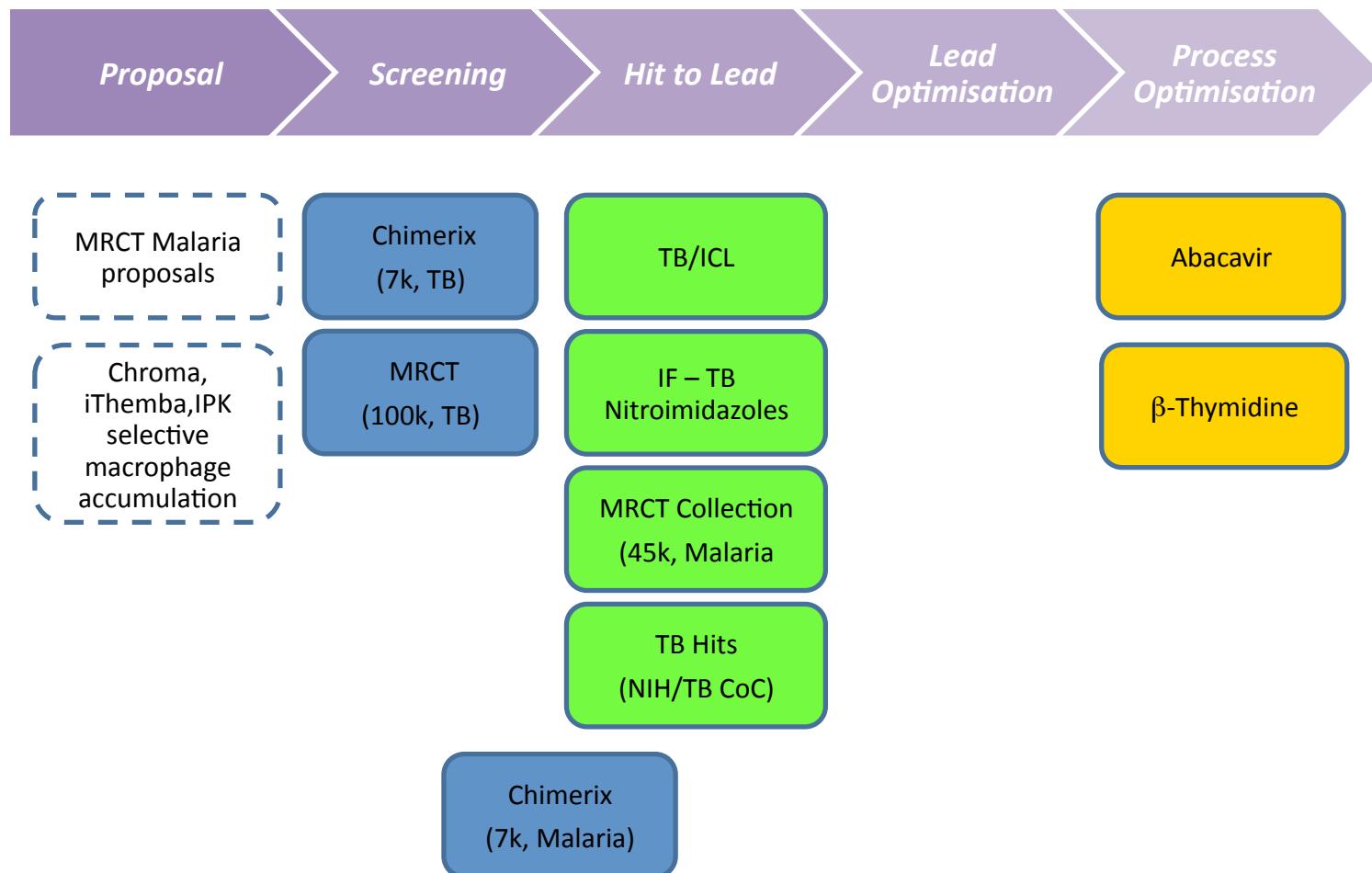
- Joint service offering with the African Institute of Biomedical Research and Technology (AiBST), Harare
 - 2h by plane
- CSO Dr. Collen Masimirembwa (PhD, DPhil)
 - >8y experience with AstraZeneca Sweden
- Offer one-stop-shop for managed medicinal chemistry
 - Deal format per sample or FTE based
- WHO-TDR DMPK Center of Excellence

Our Molecular Database

- Chemical Intermediates
 - produce and sell range of molecules



Discovery Pipeline



Drug Discovery - TB

- Highly active isocitrate lyase drug candidates
 - Best validated target for persistence
- Novel nitroimidazole drug candidates
 - Currently most exciting compounds in clinic
- Collaboration with TB CoC
 - Optimize screening hits

Drug Discovery - TB

- International consortium screening campaign to identify novel starting points
 - Phenotypic screen, 100k compounds
- Signed MOU with GSK to access Knowledge Pool for Open Innovation
 - Announced by Andrew Witty (CEO)
 - Transfer of first scientist due Jan 2011

Drug Discovery - Malaria

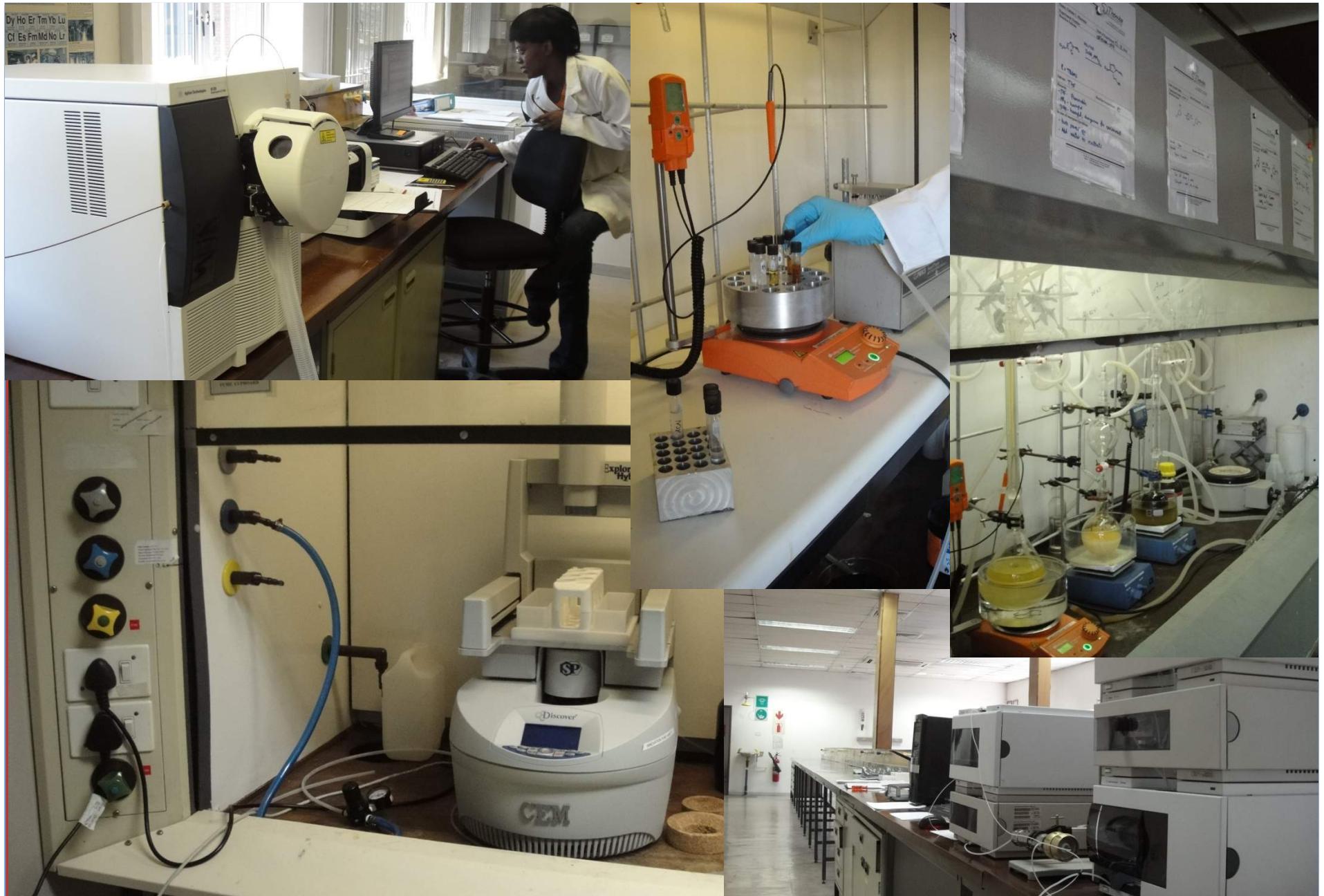
- Screening campaign complete
 - 60k compounds
- Active compounds refined
 - Properties, opportunities, potential
- Project support requested from Medicine for Malaria Venture (MMV)
 - Selected for final review (6/60), 3 to be funded

Process Technology ARV APIs

- Abacavir; alternative synthetic route licensed from Emory and investigated by iThemba
- β -thymidine and AZT; biocatalytic process which has several advantages over the existing fermentation route and could reduce cost of AZT API production

Why iThemba?

- Competitive cost base
- Strong IP laws in South Africa
- Efficient / Outcomes driven
- Access to superlative Scientific Advisory Board
- Good cultural fit
- Moral leverage – all profits re-invested into neglected disease research





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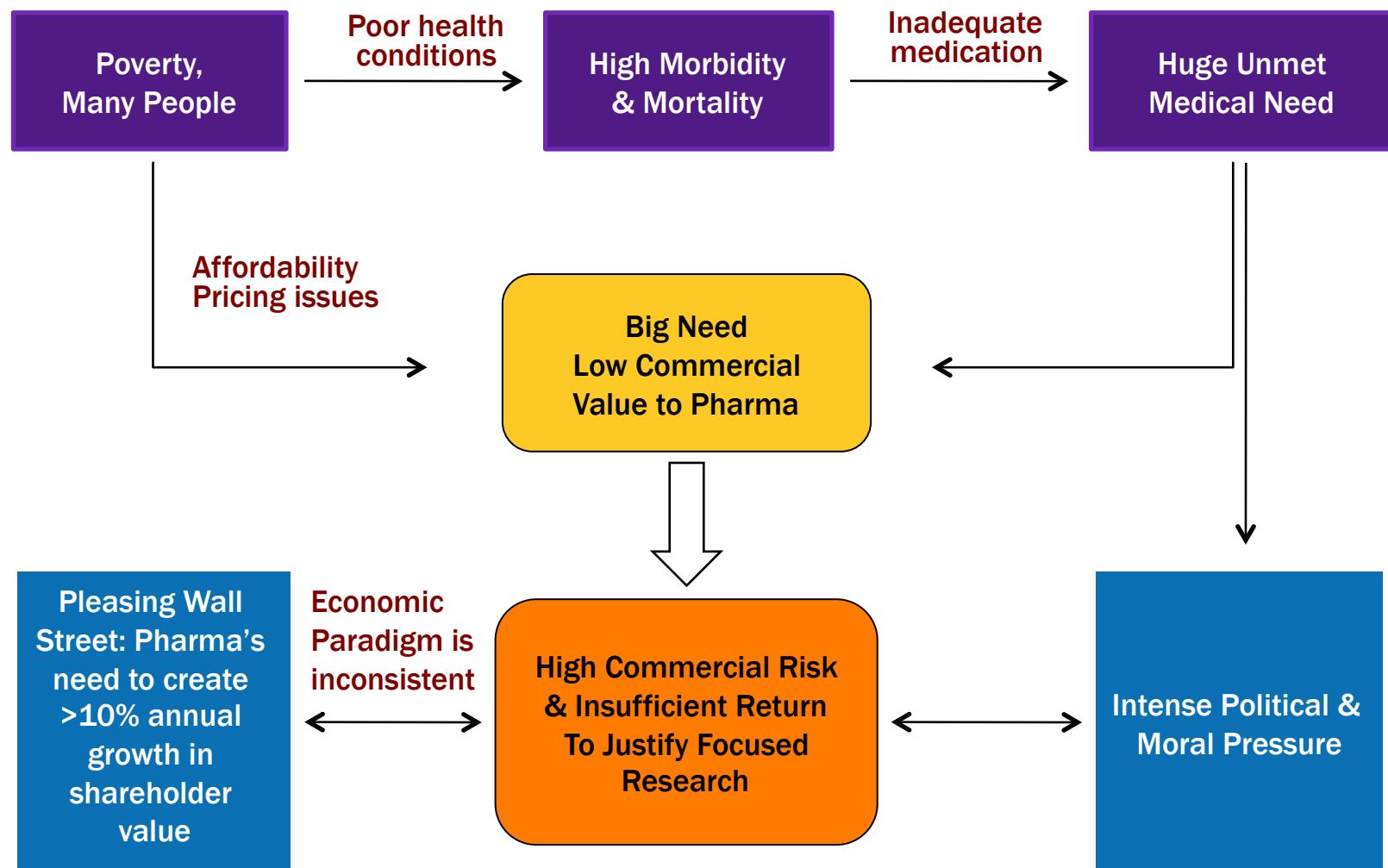
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A PROBLEM WITH PHARMA IN THE DEVELOPING WORLD



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NON-INDUSTRY PLAYERS ARE FILLING THE GAPS LEFT BY THE OLD PHARMA MODEL

- **Universities** are pursuing later stage development.
- **Governments** are providing incentives and investments.
- **Foundations** are funding research and development.
- **NGOs** are creating discovery networks.
- **Small R&D companies** are commercializing new ideas.

The New Rule

Each entity should avoid the temptation to become a FIPCO. Instead, they should focus on their strengths in the discovery/development continuum and seek partnerships with entities that possess complementary capabilities.

SCYNEXIS, INC.

- Yves Ribeill, PhD - President and CEO of SCYNEXIS, Inc.
- Over 20+ years of international pharmaceutical experience prior to SCYNEXIS, Inc.
- Member of the Scientific Advisory Committee of the World Health Organization.
- Contracted with DNDi in 2006 to discover compounds for HAT (sleeping sickness).

HIGH THROUGHPUT SCREENING: A CRITICAL ELEMENT FOR SOUTH AFRICA

- High Throughput Screening (HTS) has become an essential component for efficient and competitive drug discovery and development.
- A stand alone HTS facility without additional infrastructure to transform “hits” into clinical candidates does not represent a viable business opportunity.
- The startup costs for a national HTS facility could be easily leveraged by philanthropic contributions from foundations.
- The establishment of a South African High Throughput Screening Facility would create the opportunity for extracting maximum value from South Africa’s rich biodiversity from both an innovation and economic development perspective.