

innovation and intellectual property in drug discovery

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Chemistry, Pfizer

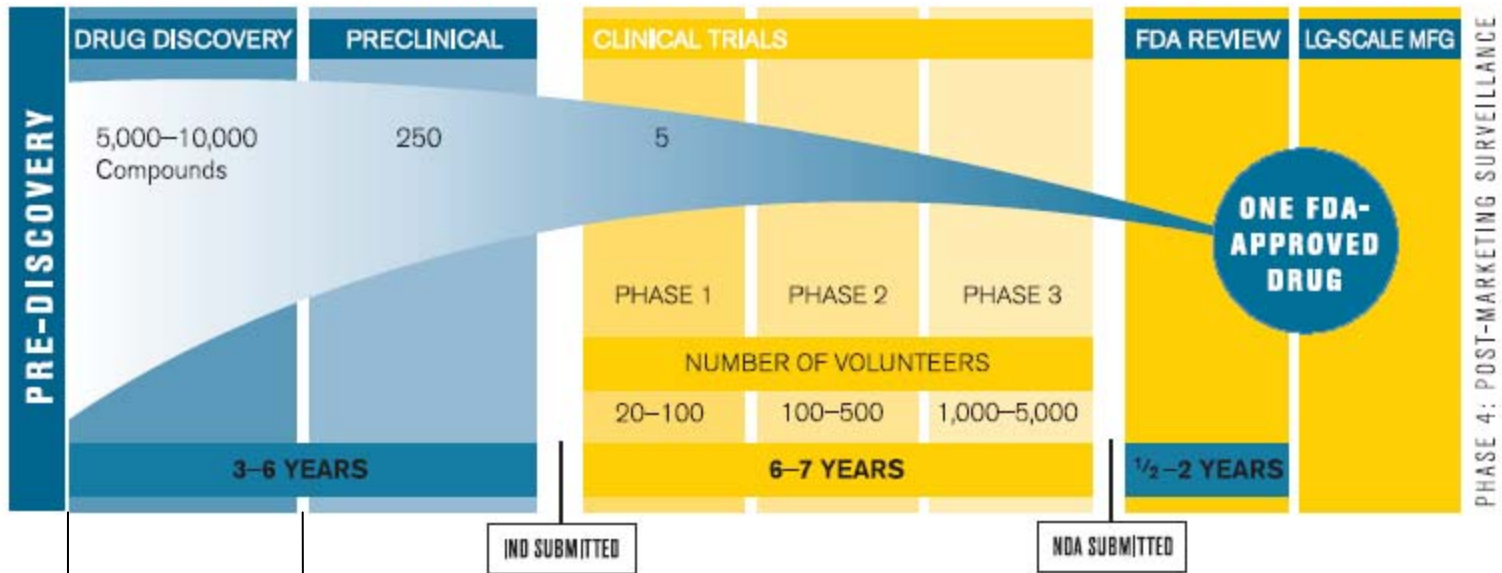


outline

- the cost and complexity of innovation in drug discovery
- attrition its relationship to disease and the need to drive molecular diversity
- the role of IP from a researchers perspective
- collaboration and open source research

R&D process summary

FIGURE 11: The R&D Process: Long, Complex, and Costly

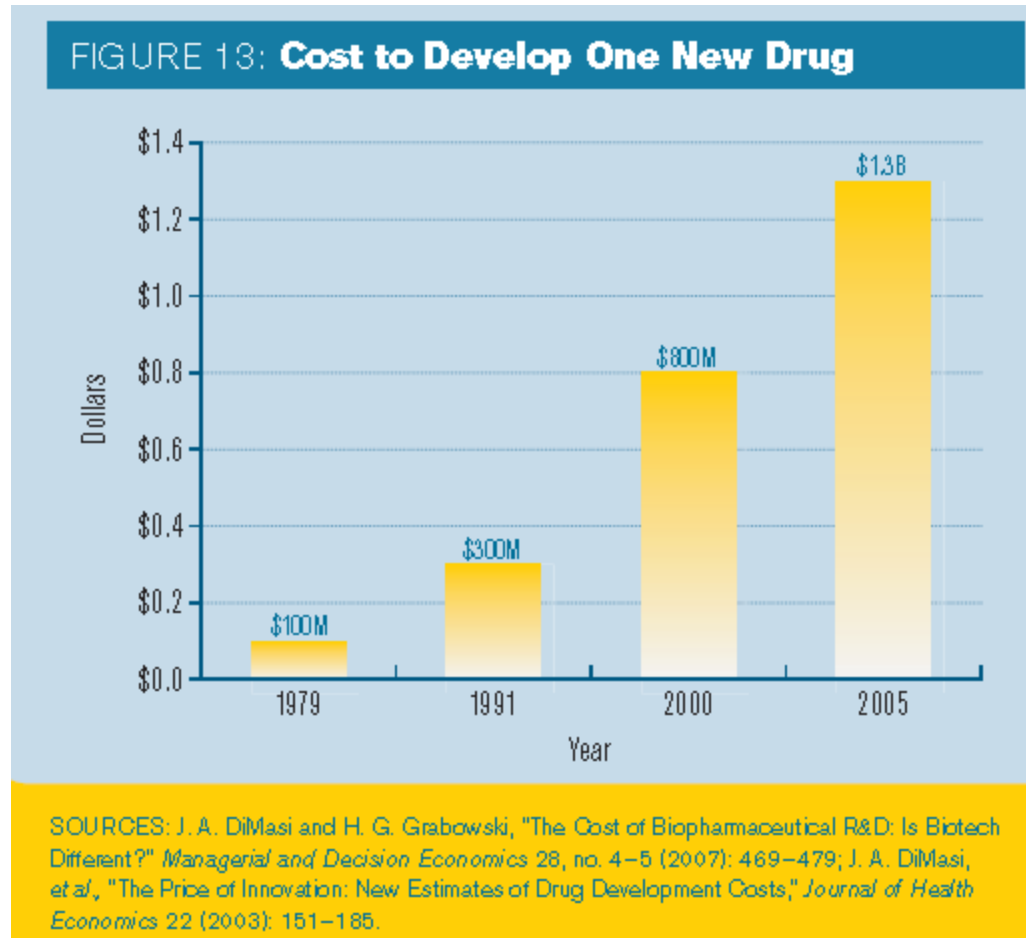


discover the right target

invent the right molecule

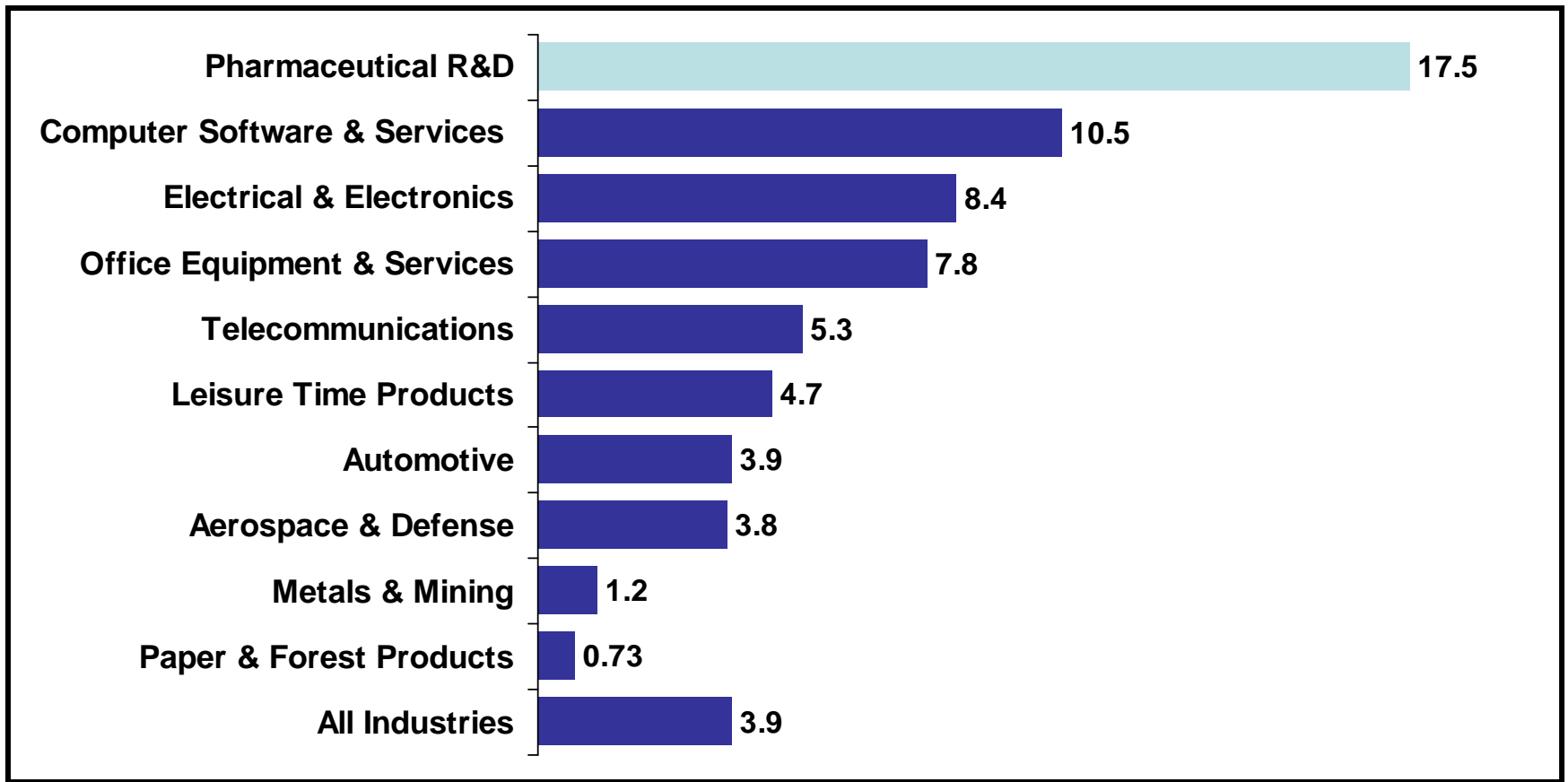


costs are increasing



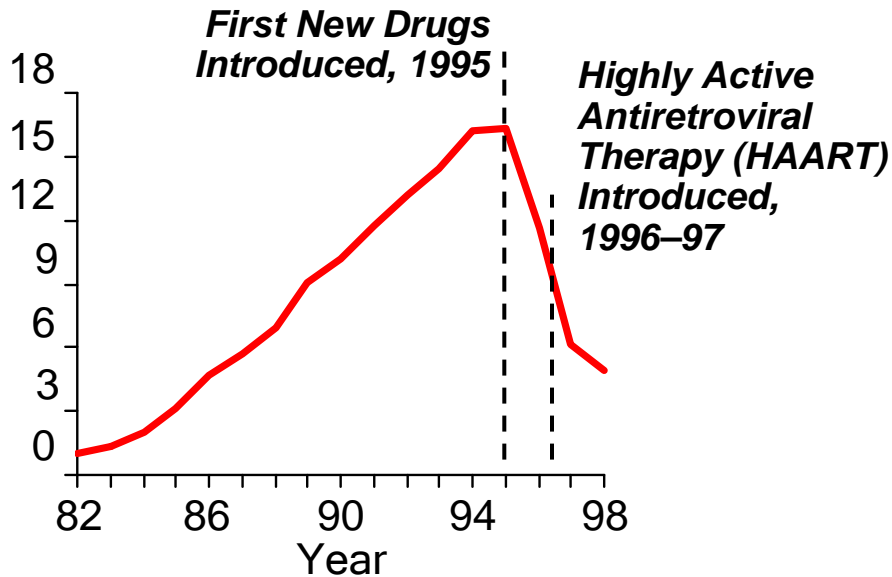
R&D expenditure

pharmaceutical and other industries
spend as percentage of annual revenues



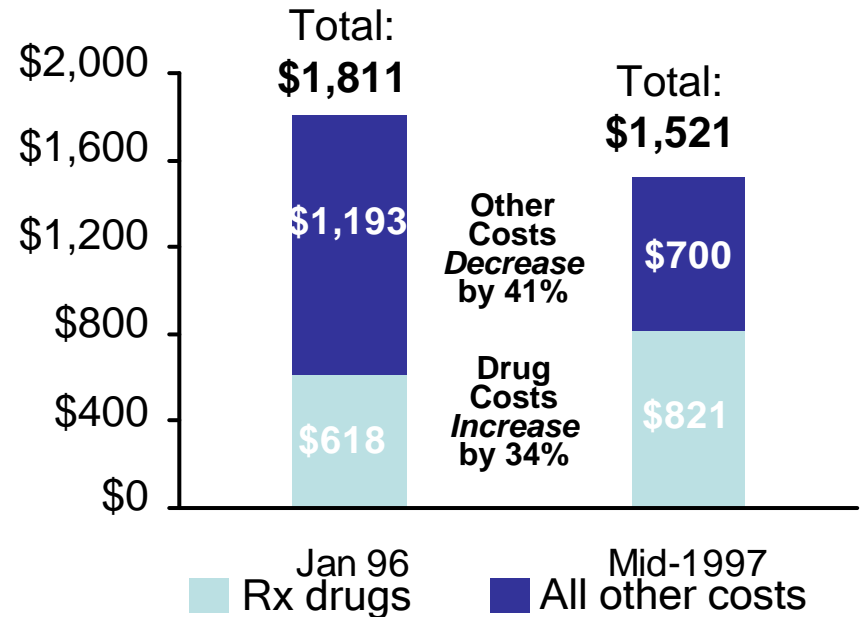
better medicines can reduce healthcare costs

AIDS Deaths per 100,000 Population



HIV Mortality Declined Dramatically After Introduction of First “Expensive” Antiretrovirals...

Monthly Health Spending for AIDS Patients

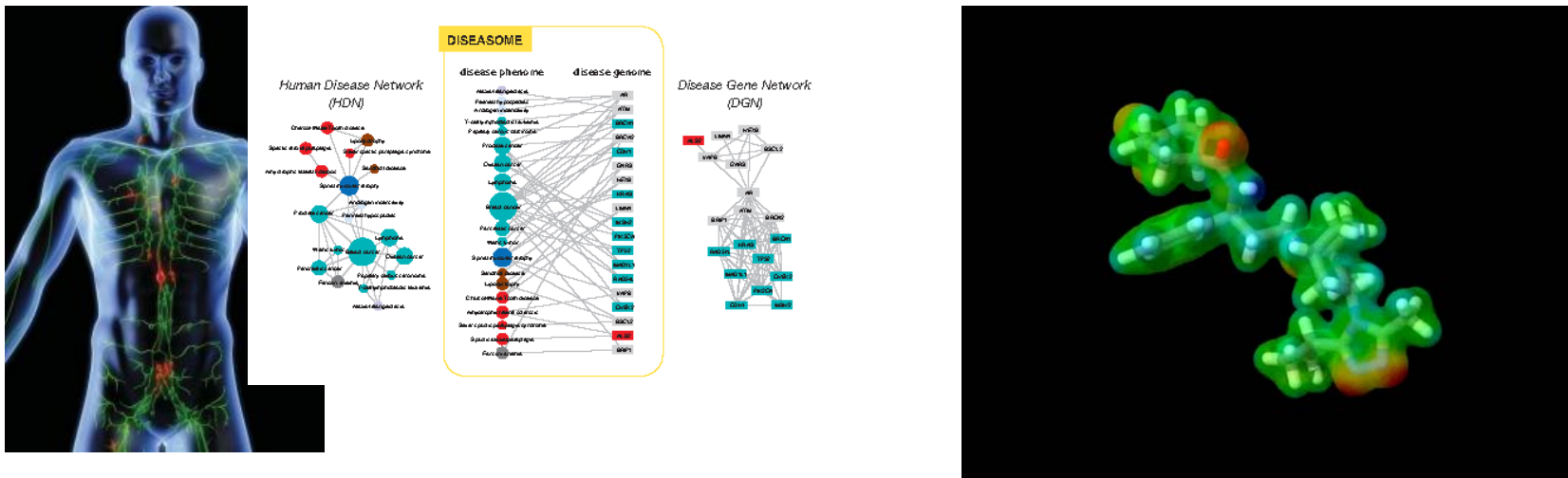


...While Monthly Costs for AIDS Patients Decreased by 16% After HAART Introduced

Sources: 1) Costs – Bozzette SA, Joyce G, McCaffrey DF, et al. Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. *New England Journal of Medicine*. 2001; 344(11):817-23; 2) Mortality – National Center for Health Statistics, Centers for Disease Control. Available at <http://www.cdc.gov/nchs>. 3) Drug development data – PhRMA and the NIH Office of Technology transfer.



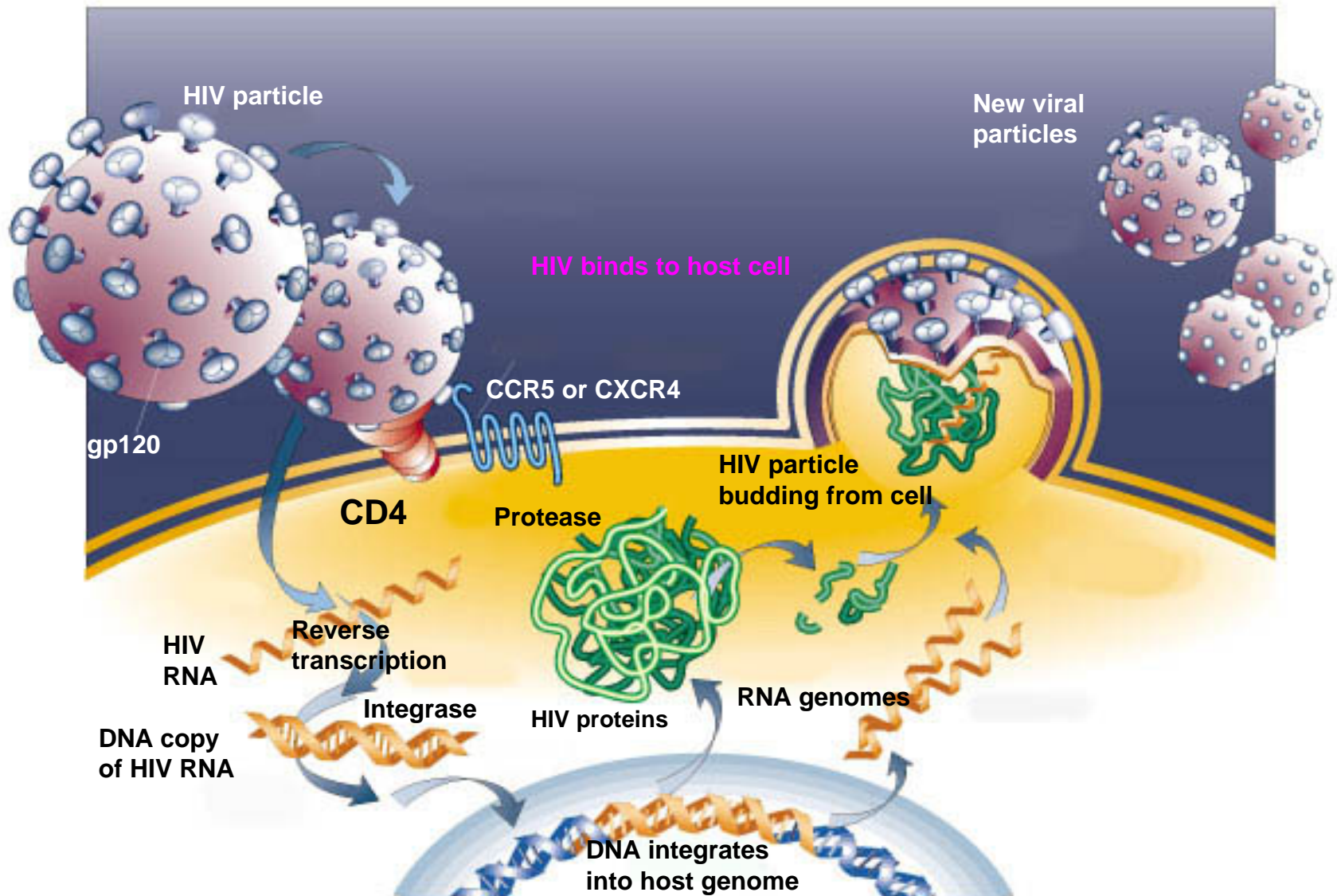
key decisions in drug discovery



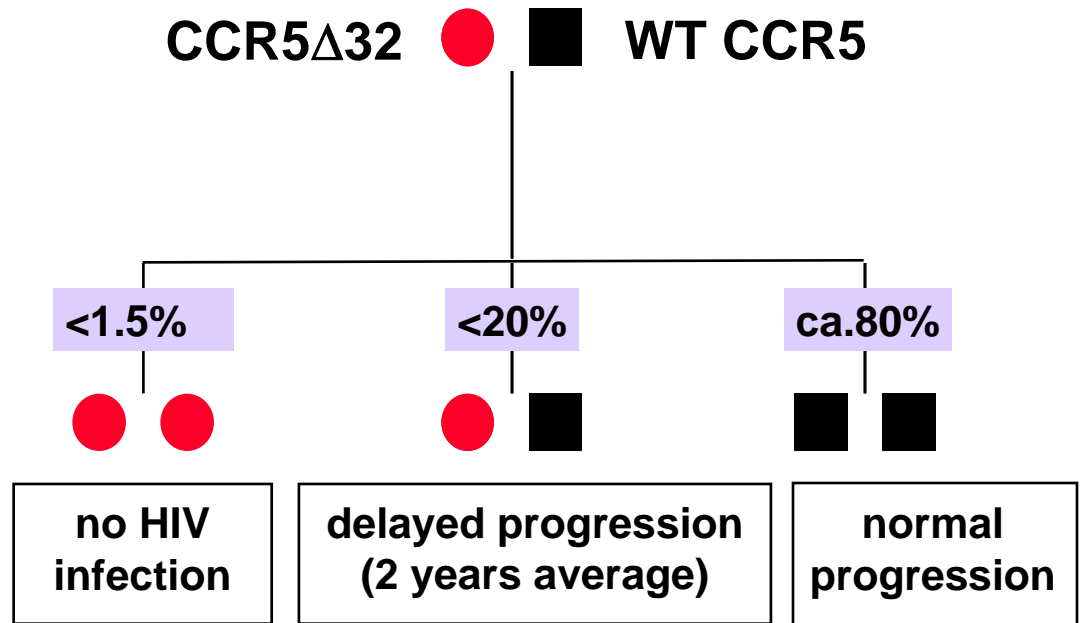
- discover the right biological target

- invent the right molecule

two examples from HIV



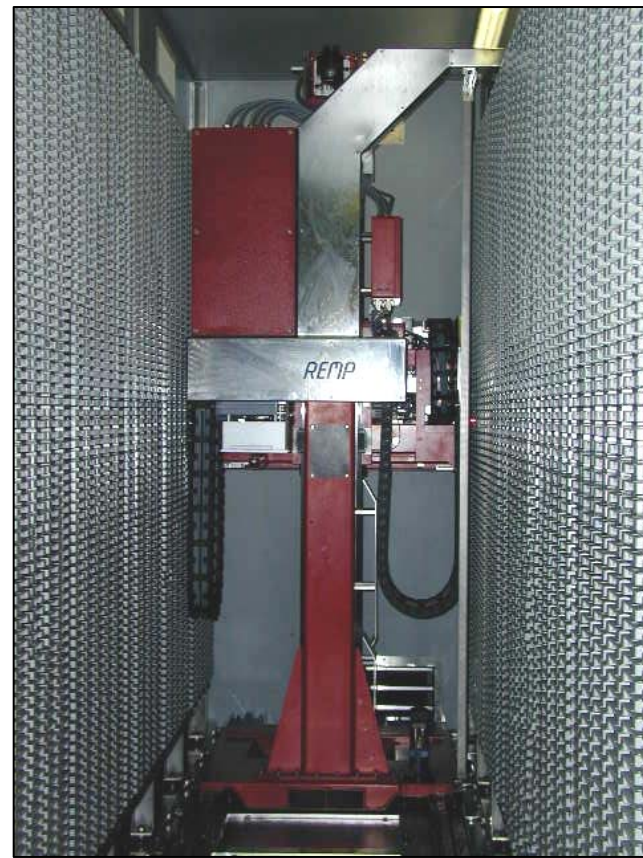
a new approach



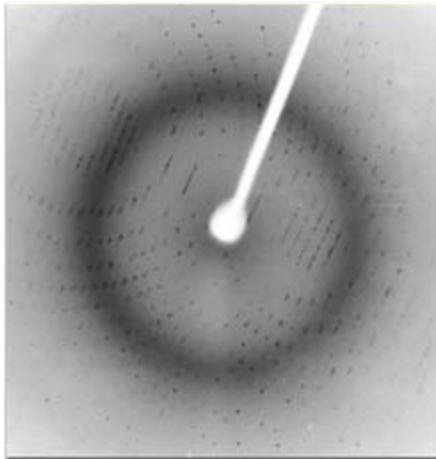
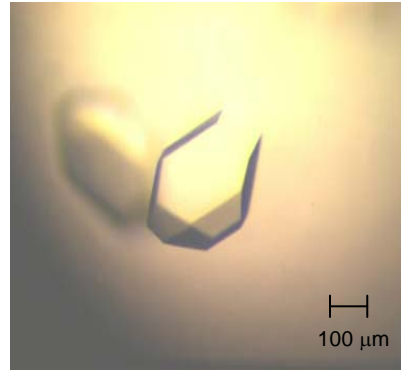
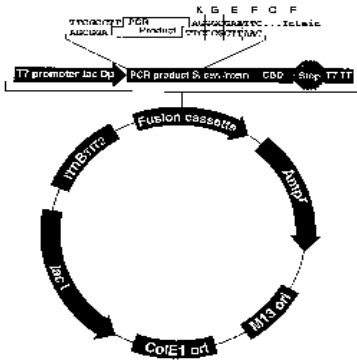
↑
improved response
to therapy

high throughput screening

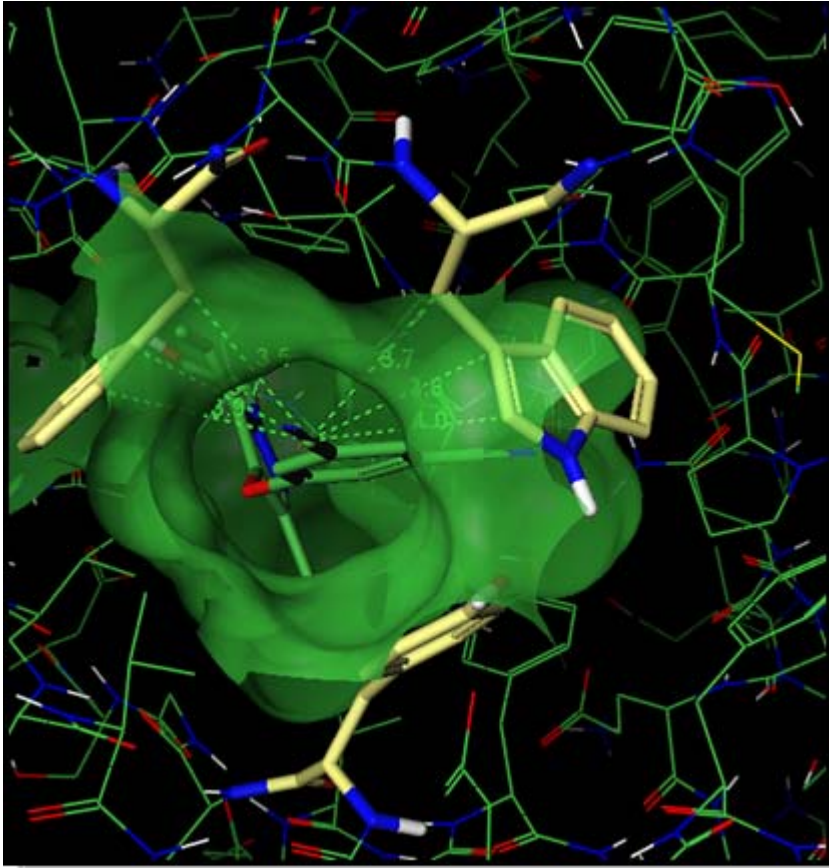
- essential tool for hit identification
- 1 million compounds tested to find a starting place



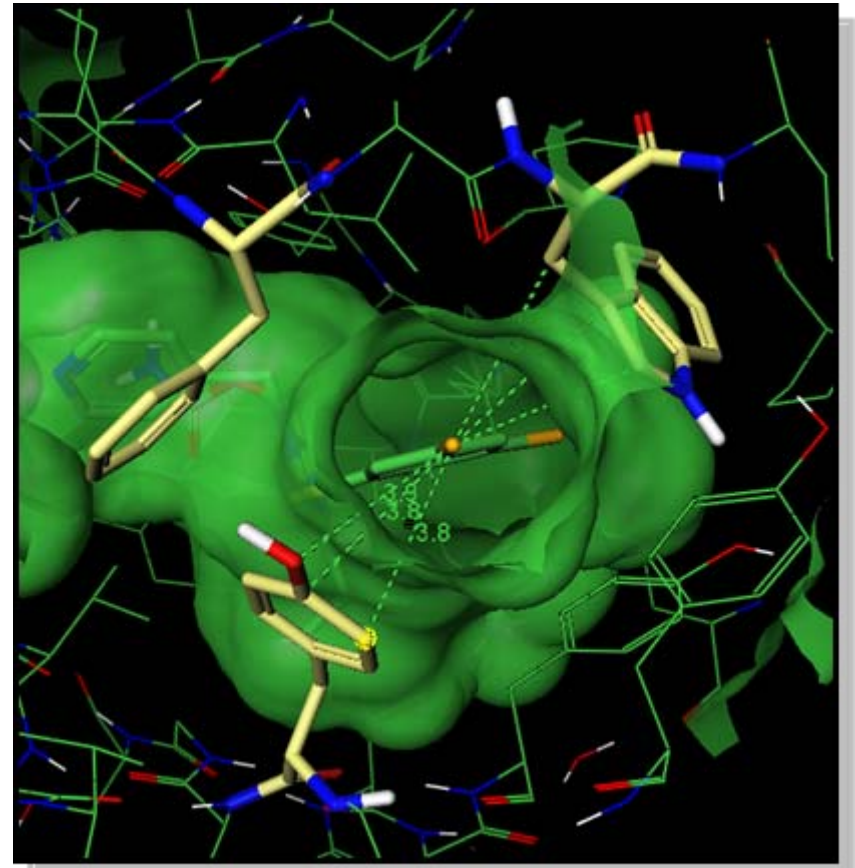
X-ray crystallography



structure based design



UK-453061/K103N RT complex
ArCN contacts to F227 & W229

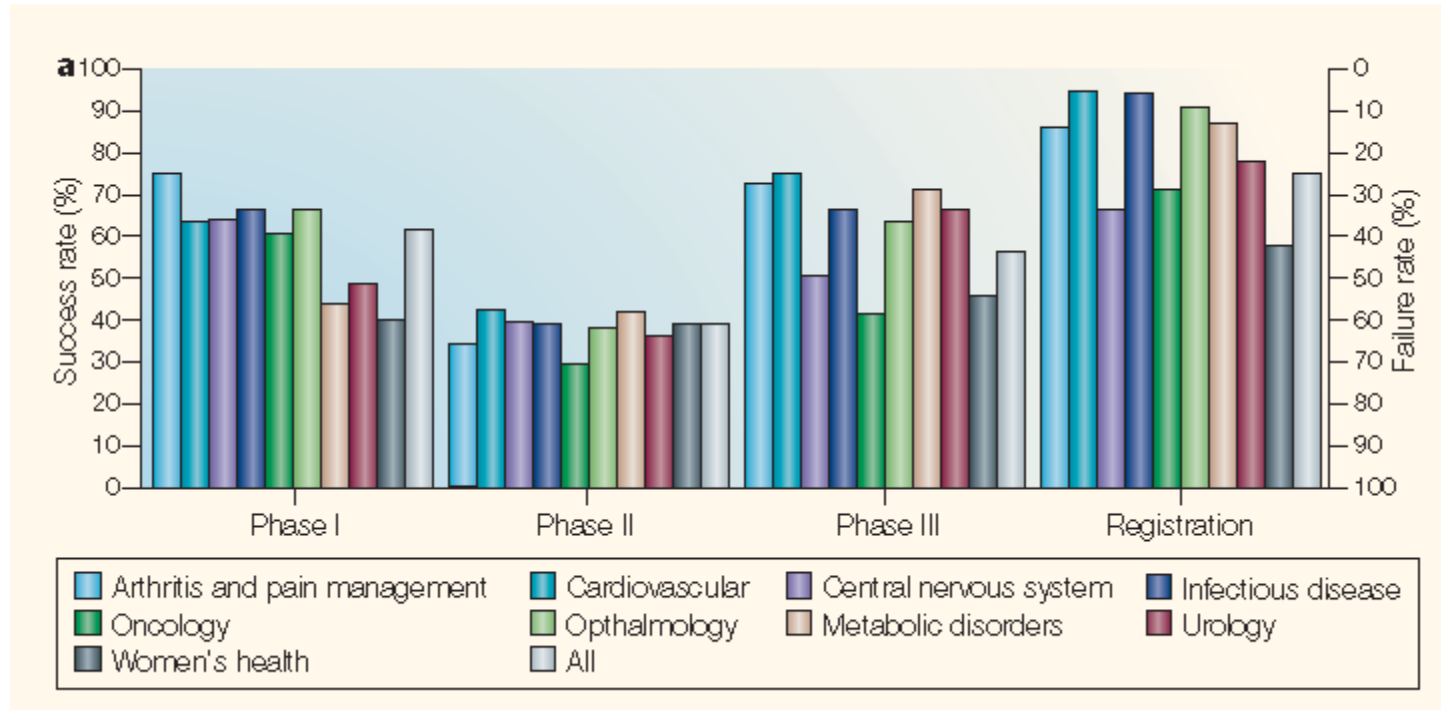


Capravirine/wt RT complex
ArCl contacts to Y188 & W229

IP supports investment

- hit identification and lead compound optimisation are technologically demanding and capital and resource intensive
- IP is essential to encourage investment in technology and drive speed through competition
- knowledge and experience are key and lead to advancement of scientific best practise through patents and publication

many approaches are needed to overcome attrition

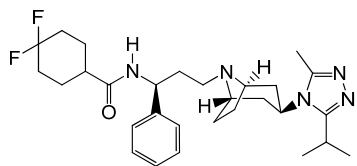


- attrition is disease agnostic

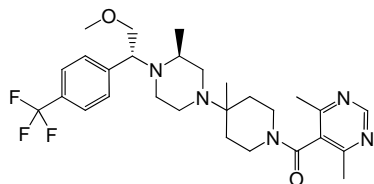
Can the pharmaceutical industry reduce attrition rates? *Ismail Kola and John Landis* NATURE REVIEWS, DRUG DISCOVERY, VOLUME 3, 2004, 711



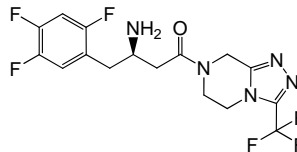
IP drives new compound diversity



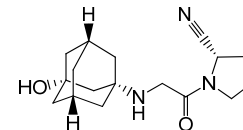
maraviroc
(Pfizer, launched)



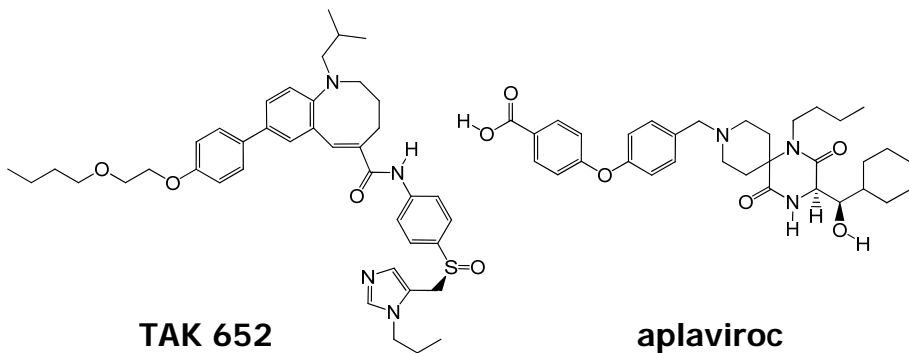
vicriviroc
(SP, PhII)



sitagliptin
(Merck, launched)



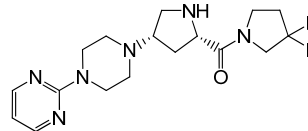
vildagliptin
(Novartis, launched)



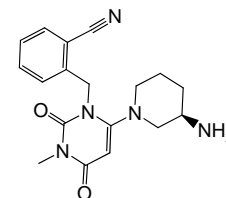
TAK 652
(Takeda, PhII)

aplaviroc
(Ono, discontinued)

CCR5 antagonists



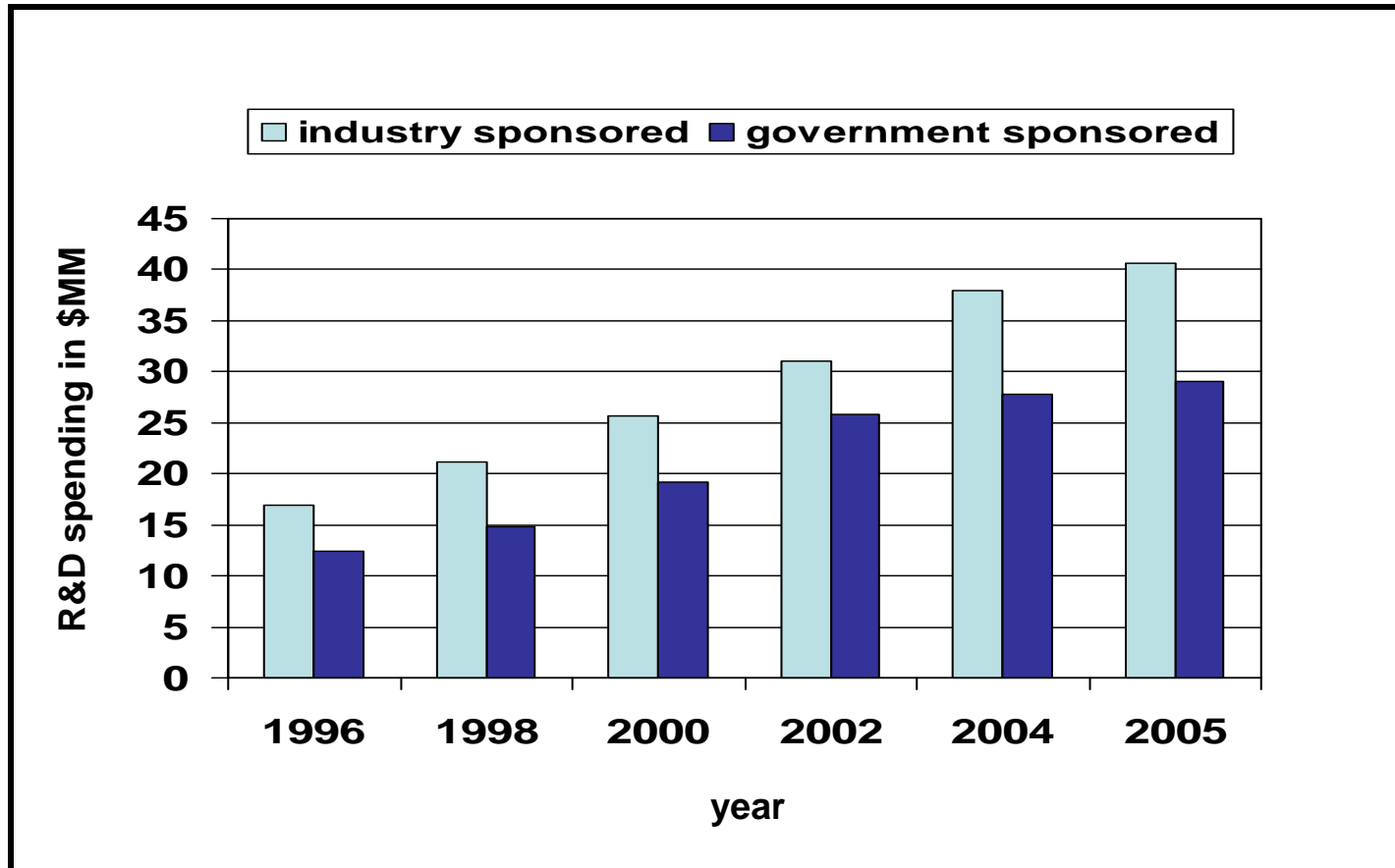
gosogliptin
(Pfizer, PhIII)



alogliptin
(Takeda, pre-registration)

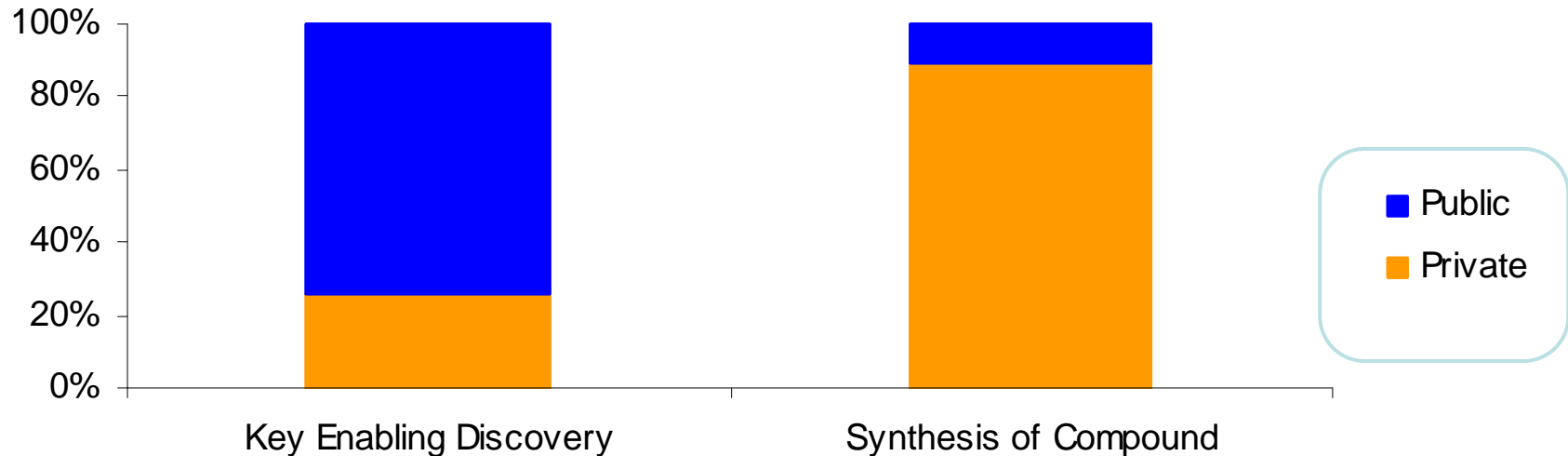
DPPIV inhibitors

R&D funding sources



who invents medicines?

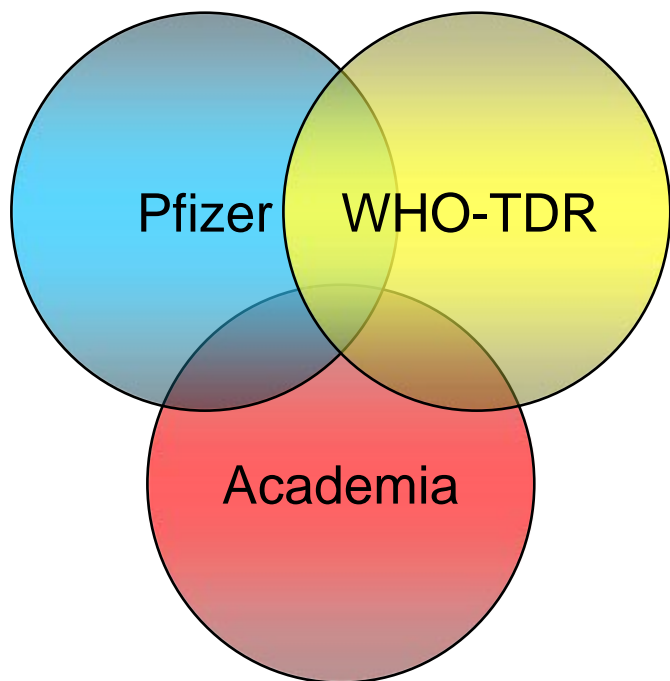
Development of the 21 Drugs with "Highest Therapeutic Value" Introduced Between 1965 and 1992



the average lag between the “key enabling discovery” and the introduction of the drug was 24 years

WHO-TDR/Pfizer collaboration

identifying novel lead compounds for tropical diseases while building scientific capacity for less developed countries



Pfizer:

PGRD Sandwich, UK

PAH Kalamazoo, MI USA

Antiprotozoal Screening:

STI, Basel – Reto Brun, Marcel Kaiser

U of Washington – Frederick Buckner

LMPH, U of Antwerp – Louis Maes

Anthelmintic Screening:

TBRI, Egypt – Fouad Yousef

NPIMR – Simon Townson

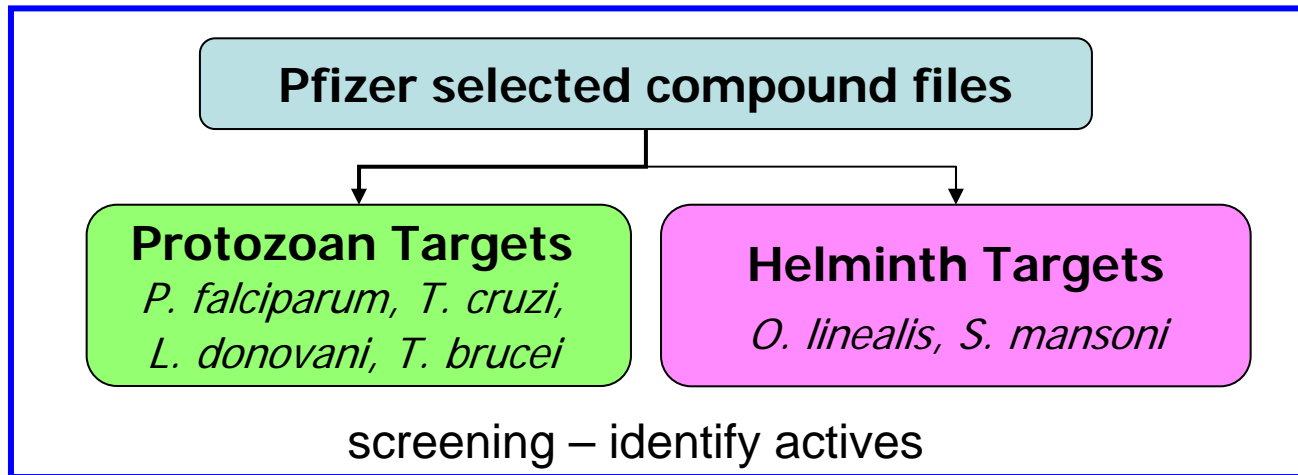
LSHTM – Quentin Bickle

New Molecular Target (GSK-3 from T. brucei)

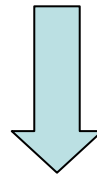
U. Of Washington – Wesley Van Voorhis



lead compound discovery activities



leverage Pfizer compound file
re-synthesize where necessary



titrate compounds for potency
test for cellular toxicity

potent, selective *in vitro* hits

exploits knowledge, skills, and resources of all partners



other achievements

- WHO-TDR Chemistry Fellow Chitalu Musonda moved to Ithemba Pharma, S. Africa in July 2008
- two manuscripts published
 - Musonda, Chitalu C., Whitlock, Gavin A., Witty, Michael J., Brun, Reto and Kaiser, Marcel 2009 "Synthesis and evaluation of 2-pyridyl pyrimidines with in vitro antiplasmodial and antileishmanial activity" *Bioorg. Med. Chem. Lett.* 19: 401-405.
 - Musonda, Chitalu C., Whitlock, Gavin A., Witty, Michael J., Brun, Reto and Kaiser, Marcel 2009 "Chloroquine-astemizole hybrids with potent in vitro and in vivo activity" *Bioorg. Med. Chem. Lett.* 19: 451-454.
- three new WHO-TDR Fellows recruited
 - Stephen Barasa (Chemistry Fellow, August 2008)
 - Silvere Ngouela (Chemistry Fellow, September 2009)
 - Richard Oduor (Biology Fellow, February 2009)
- T. brucei GSK-3 screen enabled through agreement with U. of Washington and recruitment of Biology Fellow
- pharmacologically active file (BIOPRINT) screened



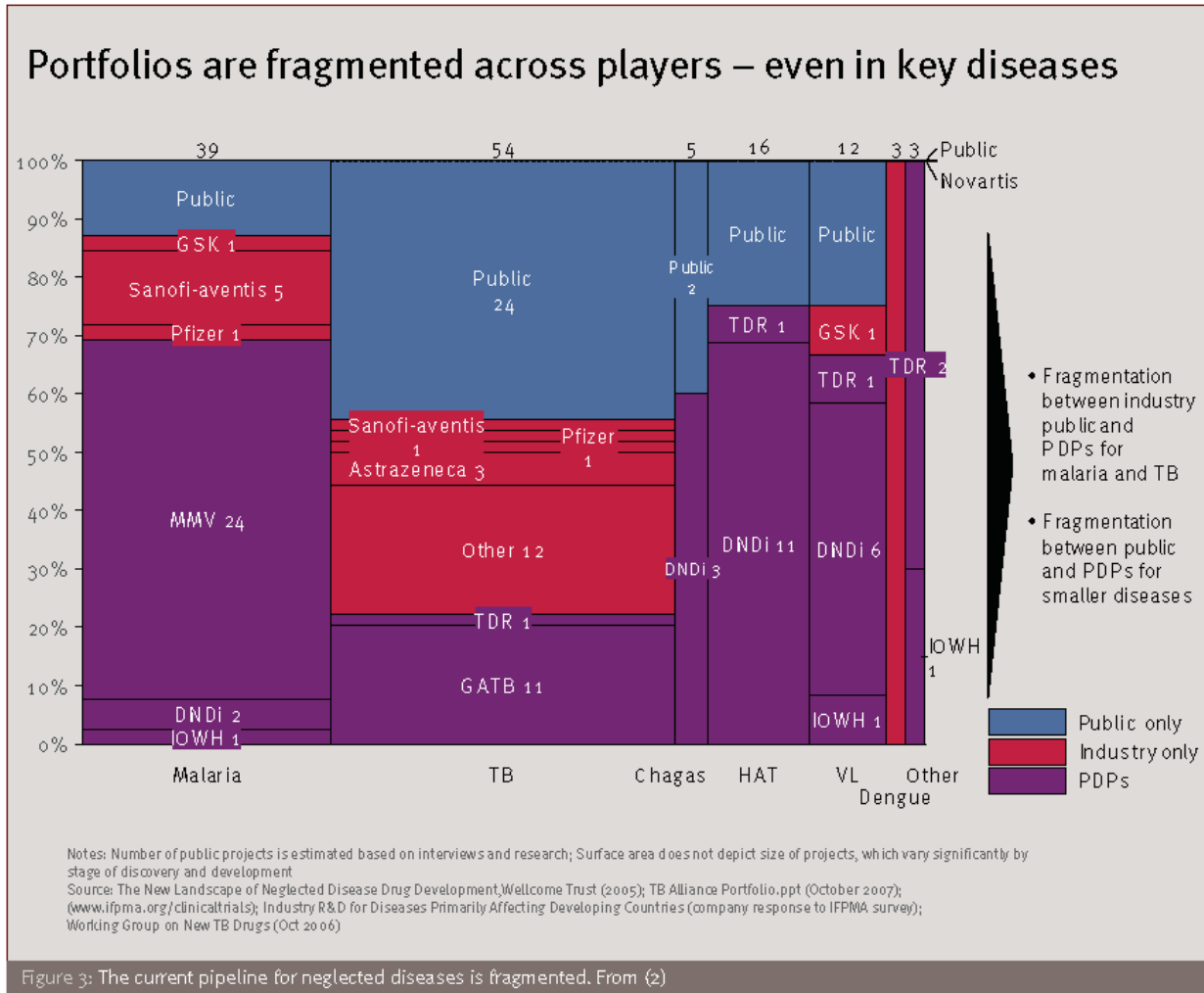
MMV/Pfizer collaboration

Medicines for Malaria Venture (MMV): not for profit organisation with mission to promote R&D of new anti-malarial drugs

- Pfizer compound library made available to MMV to screen for compounds having anti-malarial potential
- screening to be carried out at Eskitis Institute for Cell and Molecular Therapies, Griffith University, Brisbane, Australia
- upon completion of screening, Pfizer and MMV to determine which compounds are suitable for progression into potential drugs



neglected disease portfolio



- development costs will mean need for PDP and government contributions
- Herrling - Fund for R&D in Neglected Diseases (FRIND)

Source: Paul L Herrling, Global Forum Update on Research for Health, Vol 5, 152



summary

- R&D is long, complex, and costly
- IP is essential to ensure investment in technology and drive diversity and speed
- collaboration to make better use of combined resources is a potential solution
- understanding the transition between pre-competitive and competitive activities will be critical to future success