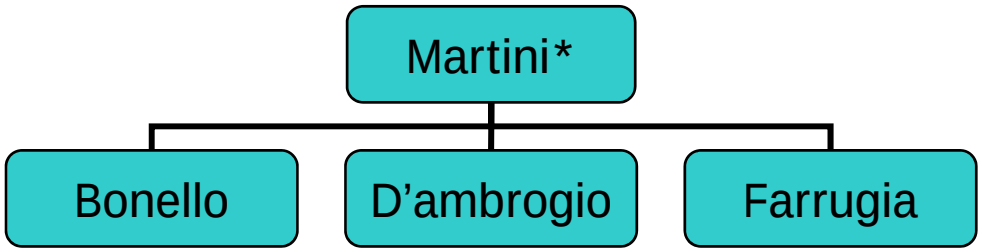
# Development Challenges facing Big Pharma & The Industrial Pharmacist

Dr Gino Martini

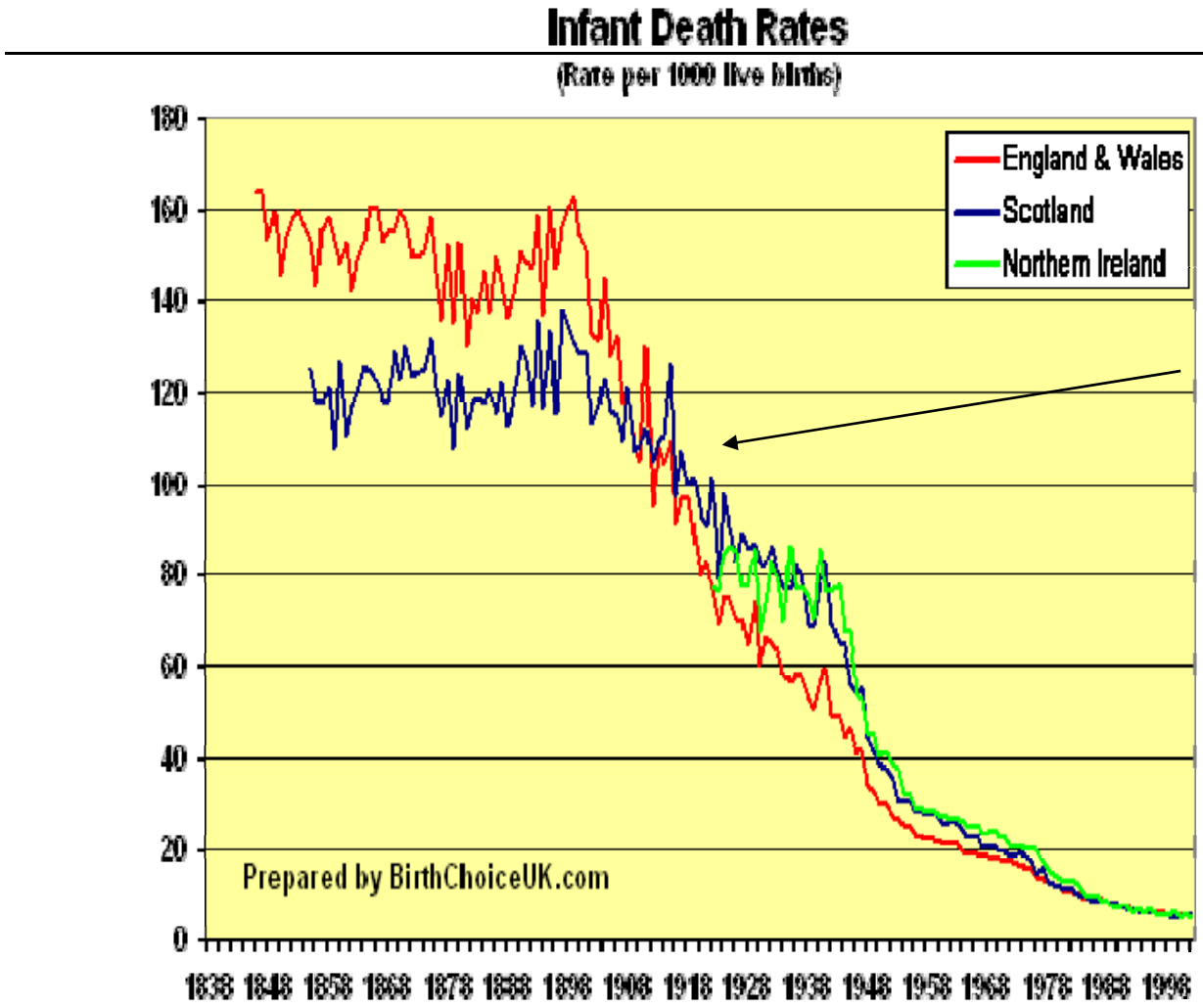
GlaxoSmithKline Pharmaceuticals

# On a Personal Note



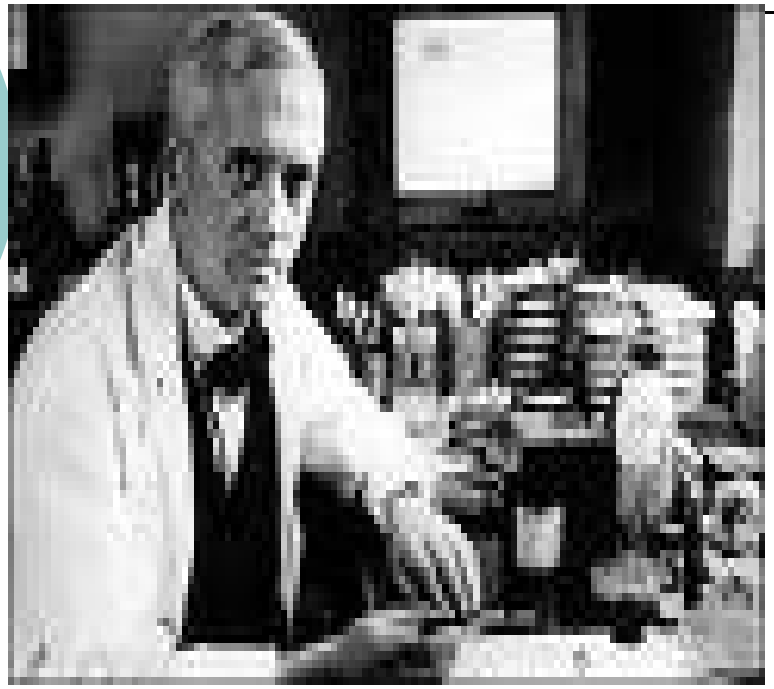

* Martini from my ancestry is linked to Baron of Malta

# Why do I enjoy being an Industrial Pharmacist?




Something happened here

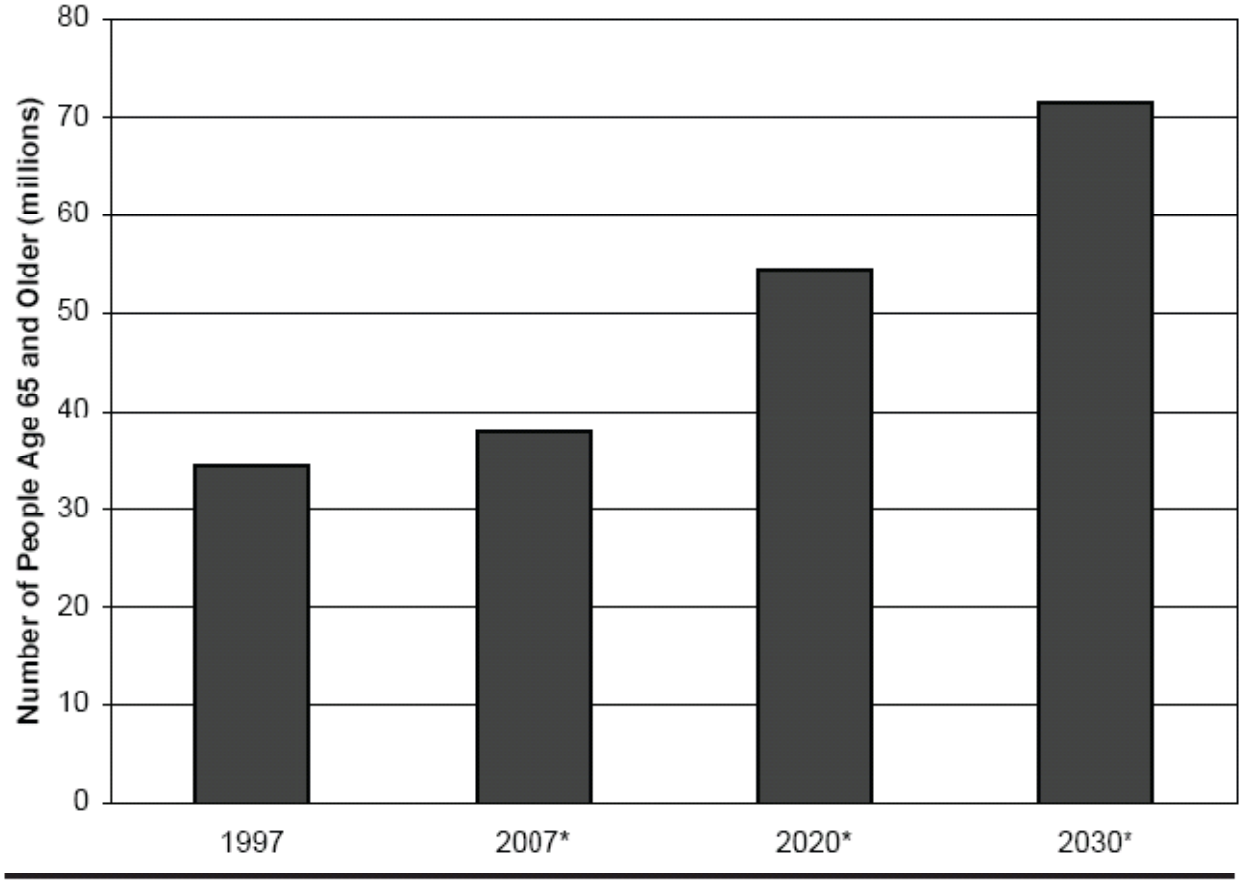
# Sir Alexander Fleming & his mouldy sandwiches!



Discovery of Pencillin & Antibiotics revolutionised medical therapy

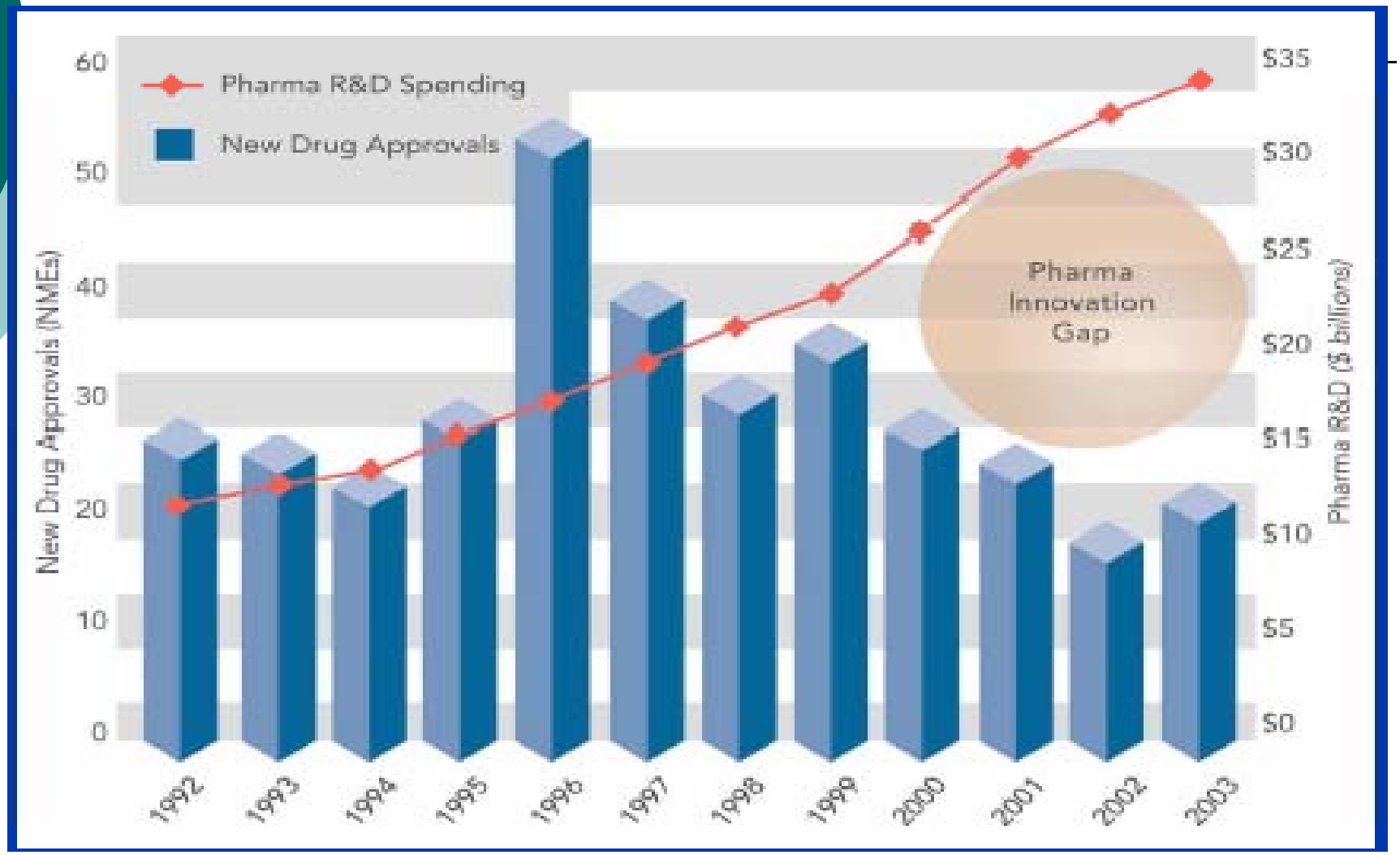
# Longevity is improving

**Number of People Over Age 65 in U.S. is Projected to Grow Rapidly**

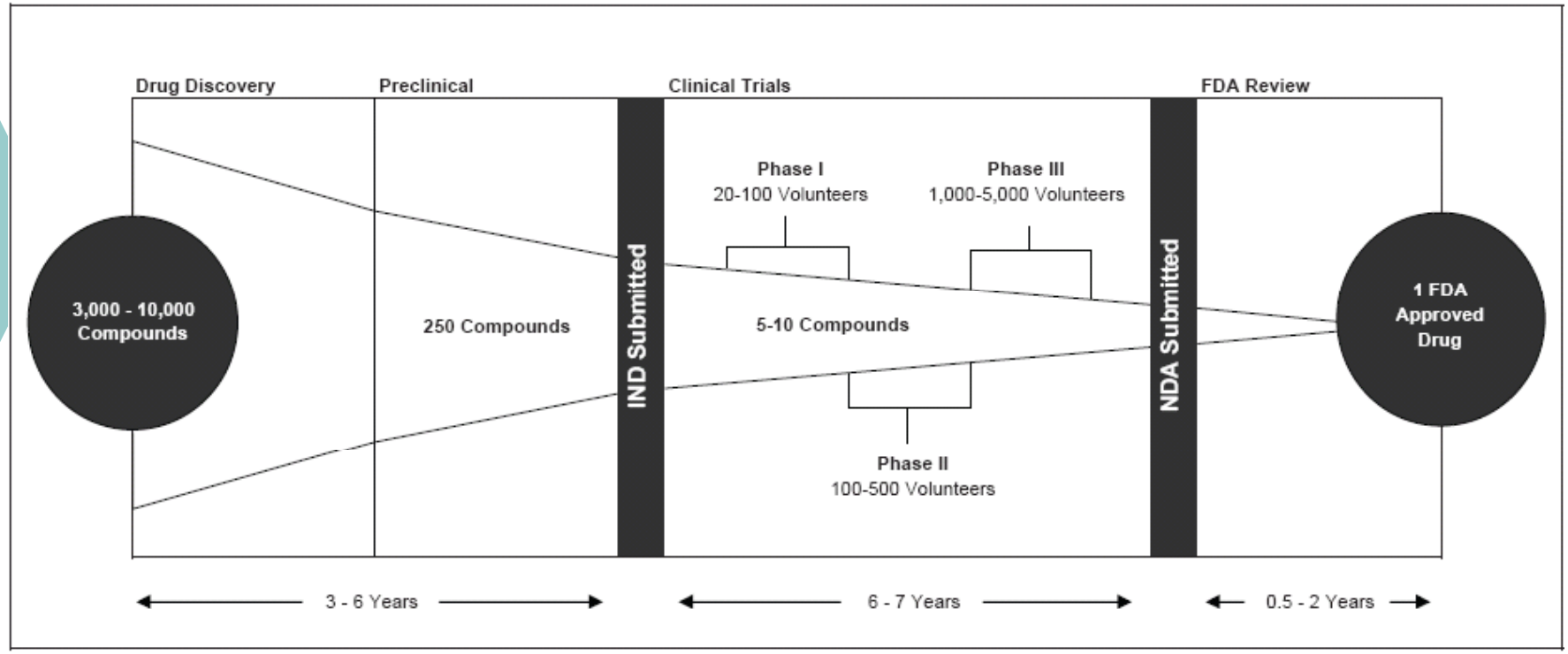



*Projected
Source: U.S. Census Bureau

# Innovation gap...



## Number of Compounds to Produce a New Drug




Source: PhRMA and FN estimates

Cost is now ~ £ 700-1billion

Success Rate 1 in 10,000

## But its not easy, the odds are not in our favour

- For every 10,000 NCE's in Discovery
  - 10 enter pre-clinical development
  - 5 enter human trials
  - 1 is approved
- Interestingly…..

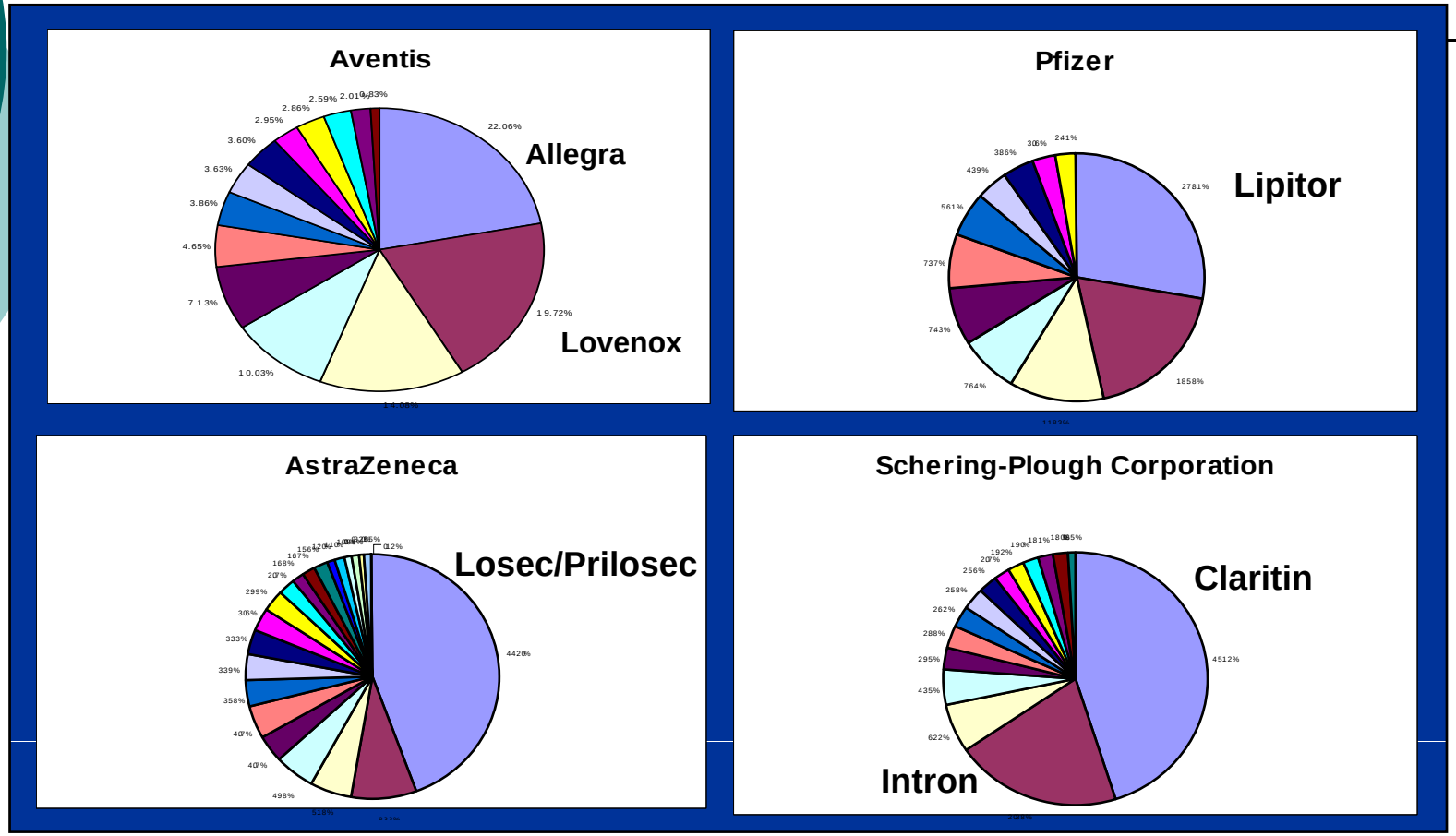
| | |
|---|---|
| Winning the lottery | 1 in 5,200,000 |
| A Royal Flush in Poker | 1 in 650,000 |
| Struck by lightning | 1 in 600,000 |
| Appear on the Tonight Show | 1 in 490,000 |
| Discovery to Market | 1 in 10,000 |
| A son who will play pro football | 1 in 8000 |

**Need Blockbusters!**

# What is a “Blockbuster”?

- Significant amount of revenue from individual product
- Minority of products drive majority of revenue
- Product appeal beyond target market
- Initial demand often exceeds capacity

# Blockbuster economics currently dominate the pharmaceutical industry




***Majority sales in their target markets***

***Alternate formulations, indications, etc beyond original target markets***

# But, only a small % of NCEs Become Blockbusters

| Sales Total Per Annum | % Achieving |
|---|---|
| **$1.8 Billion or >** | **1.0%** |
| $920 Million - $1.8 Billion | 1.0% |
| $460 Million - $920 Million | 2.0% |
| $180 Million - $460 Million | 6.0% |
| < $180 Million | 90.0% |

Average for all Drugs -- $265 Million per Annum

***Sources: PriceWaterhouse Coopers, SCRIP***

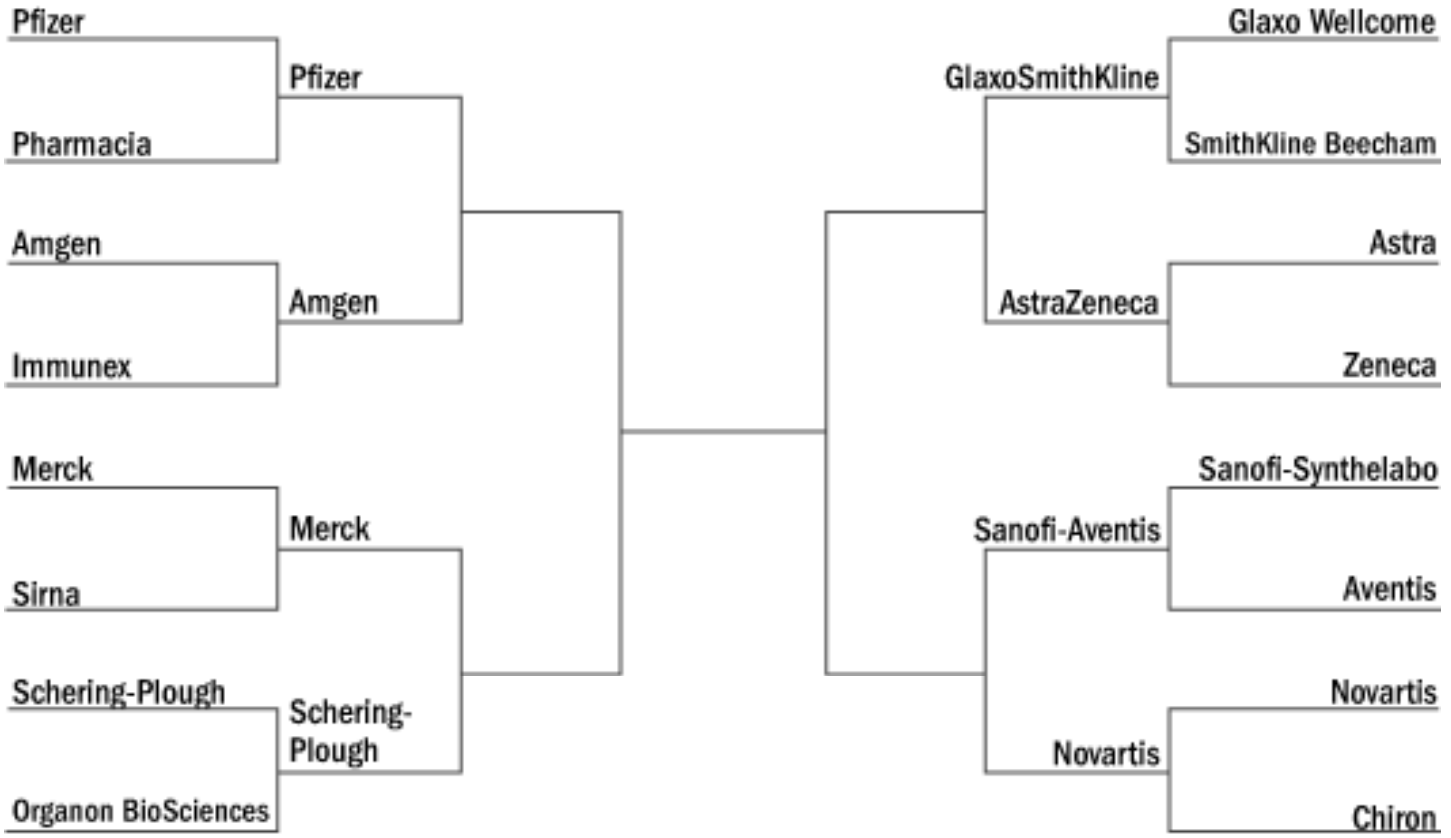
# Revenue and Patent Expiration of Top 12 Pharmaceuticals

| Drug | Company | 1997 Revenue in $ Millions | Patent Expiration |
|---|---|---|---|
| Zocor | Merck | 3,575 | 2005 |
| Losec | Astra | 2,816 | 2001 |
| Prozac | Eli Lilly | 2,559 | 2001 |
| Augmentin | SmithKline Beecham | 1,517 | 2002 |
| Zoloft | Pfizer | 1,507 | 2005 |
| Paxill | SmithKline Beecham | 1,474 | 2005 |
| Cipro | Bayer | 1,441 | 2004 |

**$82 billion worth of global blockbusters will have lost US patent protection by 2007**

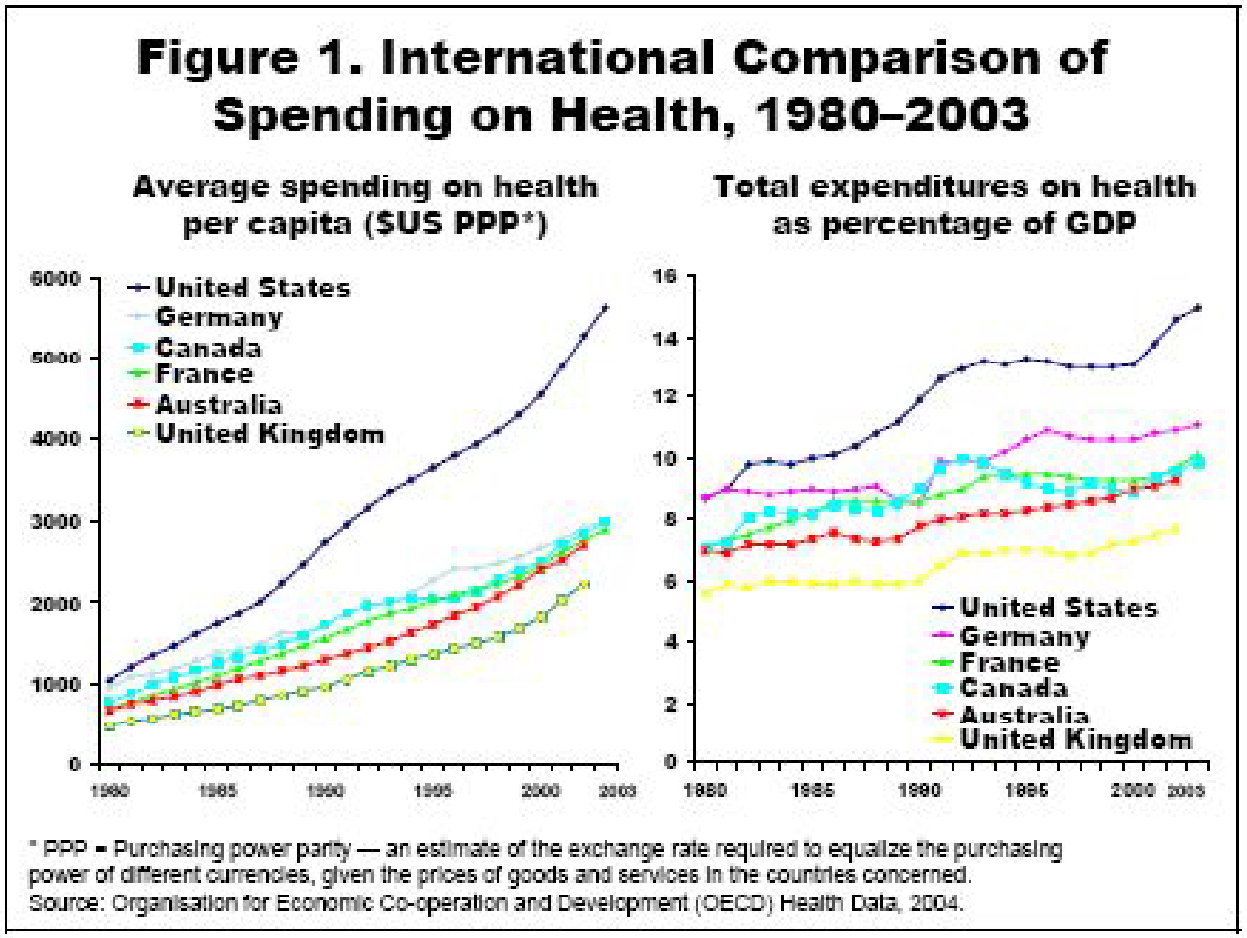
Note: * Includes alliances with values estimated to be greater than $20M including up-front payments, equity, R&D funding, and contingent milestone payments
Sources :Recombinant Capital, MedAd News

# Old Paradigm was to beef up



# Relying on Blockbusters is ‘risky business’ in these meta analysis days!

# High Healthcare Costs



# Now outstripping Defense Spend

| COUNTRY | Country Data | | | Defence Expenditure - 2004 | | | Foreign Aid - 2003 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Population (2004) | GDP (2003) ($US billions) | GDP (2004) ($US billions) | US$ (billions) | US$ per capita | % of GDP | US$ (billions) | US$ per capita | % of GDP |
| Argentina | 38,377,000 | 129.60 | 151.50 | 1.60 | $42 | 1.06% | n/a | n/a | n/a |
| Australia | 19,890,000 | 522.40 | 631.30 | 11.70 | $588 | 1.85% | 0.51 | $25.39 | 0.10% |
| Brazil | 174,471,000 | 505.70 | 604.90 | 9.20 | $53 | 1.52% | n/a | n/a | n/a |
| **Canada** | **31,630,000** | **856.50** | **979.80** | **10.10** | **$319** | **1.03%** | **2.03** | **$64.21** | **0.24%** |
| China | 1,288,400,000 | 1,400.00 | 1,600.00 | 25.00 | $19 | 1.56% | n/a | n/a | n/a |
| France | 59,725,000 | 1,800.00 | 2,000.00 | 40.00 | $670 | 2.00% | 7.25 | $121.44 | 0.40% |
| Germany | 82,551,000 | 2,400.00 | 2,700.00 | 29.70 | $360 | 1.10% | 6.78 | $82.18 | 0.28% |
| India | 1,064,399,000 | 600.60 | 691.90 | 19.10 | $18 | 2.76% | n/a | n/a | n/a |
| Indonesia | 214,471,000 | 238.50 | 257.60 | 2.30 | $11 | 0.89% | n/a | n/a | n/a |
| Italy | 57,646,000 | 1,500.00 | 1,700.00 | 17.50 | $304 | 1.03% | 2.43 | $42.21 | 0.16% |
| Japan | 127,210,000 | 4,300.00 | 4,600.00 | 2.30 | $18 | 0.05% | 8.88 | $69.81 | 0.21% |
| Korea (South) | 47,912,000 | 608.10 | 679.70 | 16.40 | $342 | 2.41% | 0.28 | $5.82 | 0.05% |
| Mexico | 102,291,000 | 639.10 | 676.50 | 2.80 | $27 | 0.41% | n/a | n/a | n/a |
| Russia | 143,425,000 | 430.10 | 582.40 | 14.20 | $99 | 2.44% | n/a | n/a | n/a |
| Saudi-Arabia | 22,528,000 | 212.60 | 250.60 | 19.30 | $857 | 7.70% | n/a | n/a | n/a |
| South Africa | 45,294,000 | 165.40 | 212.80 | 3.30 | $73 | 1.55% | n/a | n/a | n/a |
| Turkey | 70,712,000 | 240.40 | 301.90 | 8.50 | $120 | 2.82% | n/a | n/a | n/a |
| United Kingdom | 59,280,000 | 1,800.00 | 2,100.00 | 49.00 | $827 | 2.33% | 6.28 | $105.97 | 0.35% |
| United States | 291,044,000 | 10,900.00 | 11,700.00 | 460.50 | $1,582 | 3.94% | 16.25 | $55.85 | 0.15% |

**SOURCES**

**Population** The International Institute For Strategic Studies, *The Military Balance 2004-2005* (London: Oxford University Press, 2005).

**GDP** World Bank, World Development Indicators database, Updated 15 July 2005, available at: http://www.worldbank.org/data/countryda

**Defence Spendir** *The Military Balance 2004-2005*

**Foreign Aid** Data for all countries except South Korea and Saudia Arabia comes from the OECD, Development Co-operation Directorate, "FINAI Where Foreign Aid data is unavailable, it is because no data could be found or the country is a net recipient of Foreign Aid accordir

**Calculations** Foreign aid spending per capita and as a % of GDP was calculated based on the most recent available data on ODA (2003) and co Defence spending per capita and as a % of GDP was calculated based on the most recent available data on defence expenditures (

**NOTE:** There are 19 nation state members of the G-20. The 20th member, European Union, is not represented here.

**THESE CALCULATIONS ARE ESTIMATIONS ONLY.**

GPIE EIPG

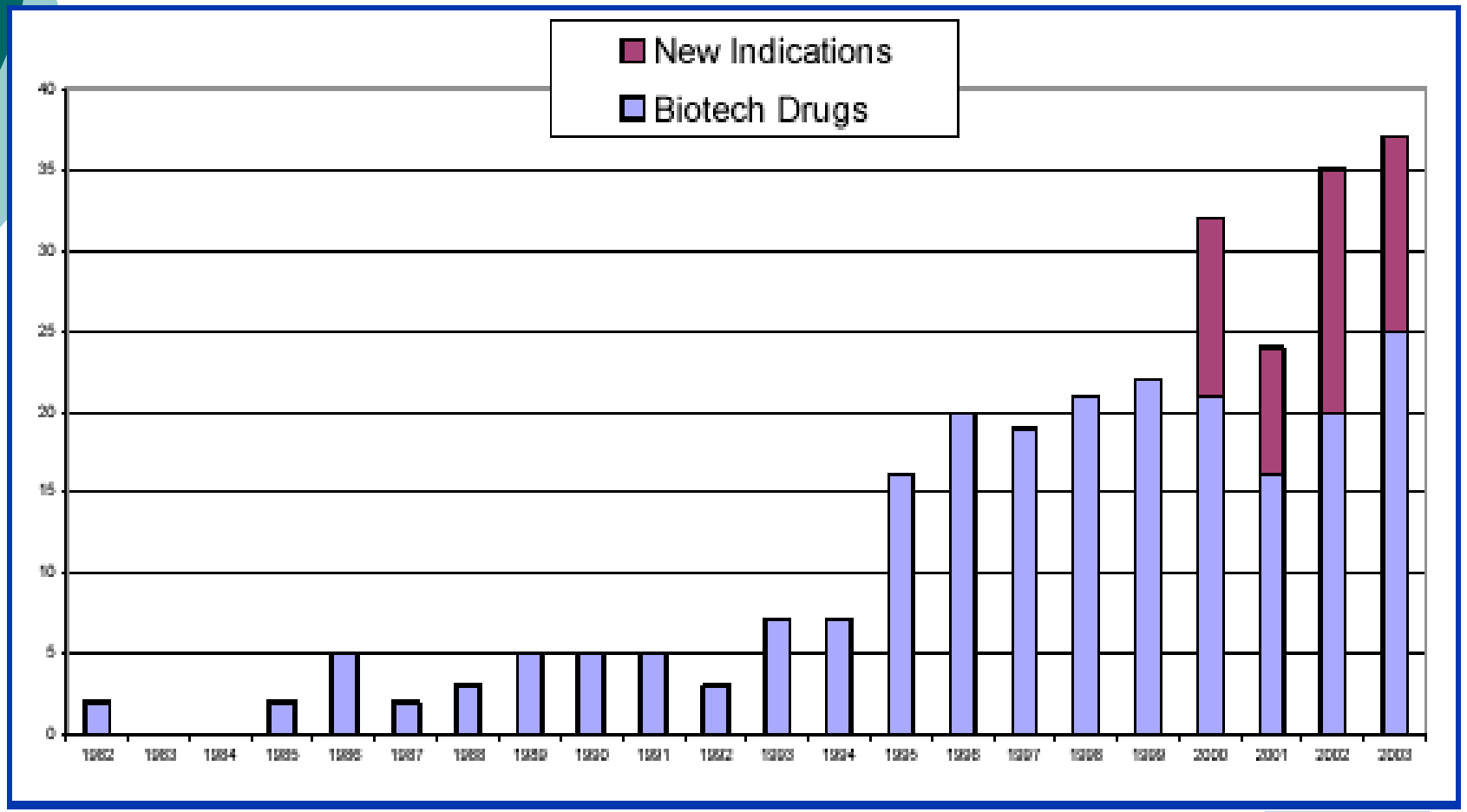
# Big pharma challenges…

- ✓ R&D spending growing faster than sales growth
- ✓ New product discoveries lagging relative to industry growth needs
- ✓ Need for licensing products from outside Core Expertise!

*“By 2010 most pharmaceutical research will be undertaken by biotechnology companies”*

**Deutsche Bank**

# Number of biotech products approved



# Biotech - Big pharma Alliances

Biotech does some things very well (invent, proteins, niche)

Big pharma does some things very well (develop, market, sell)

Must overcome NIH

As with any marriage, both parties must nurture the relationship

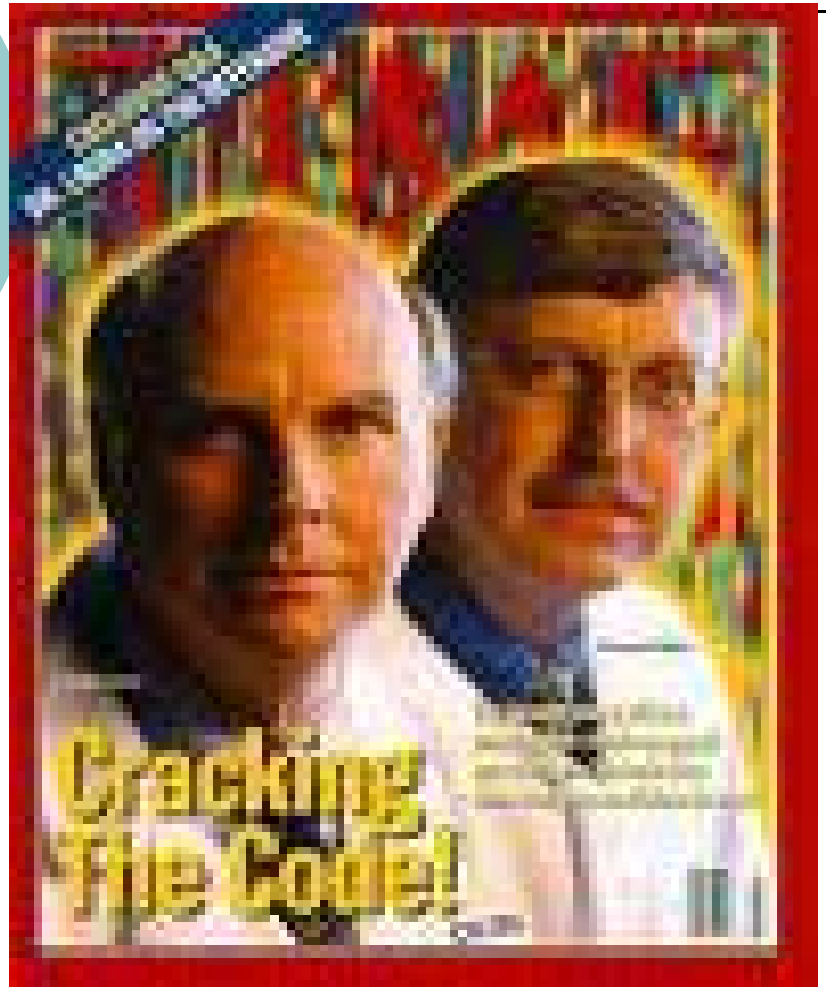
Big companies like small molecules,

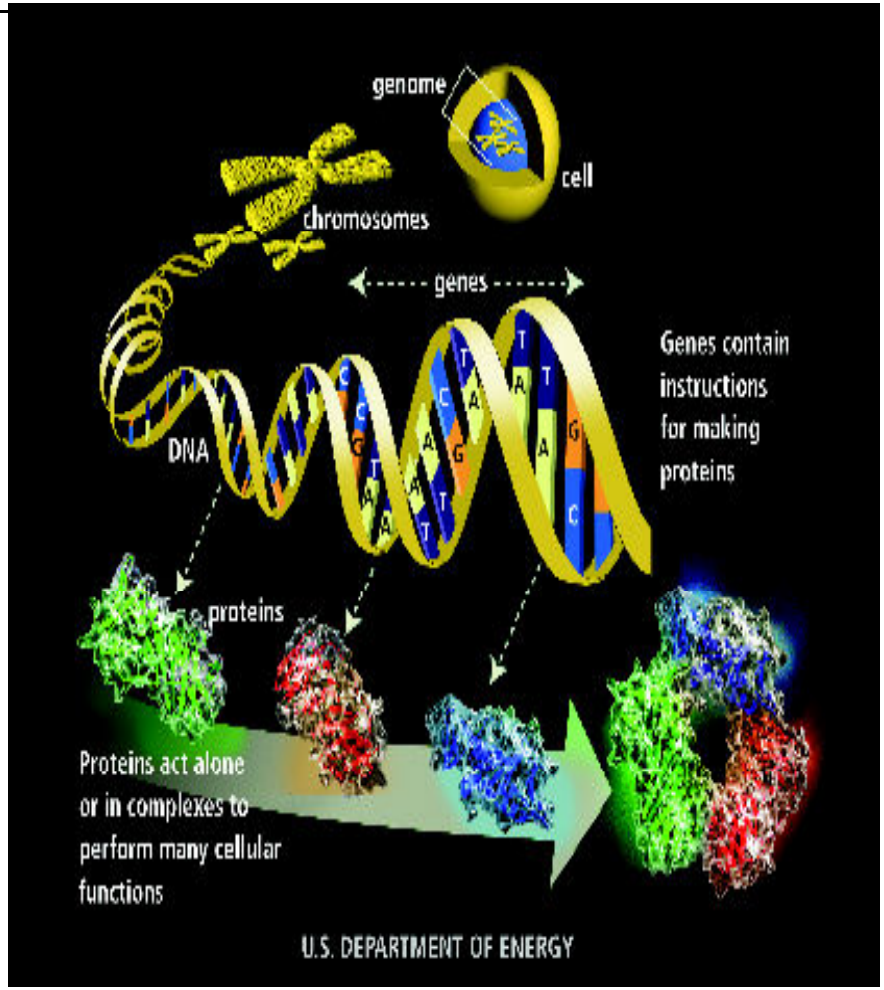
small companies like big molecules.

Judah Folkman

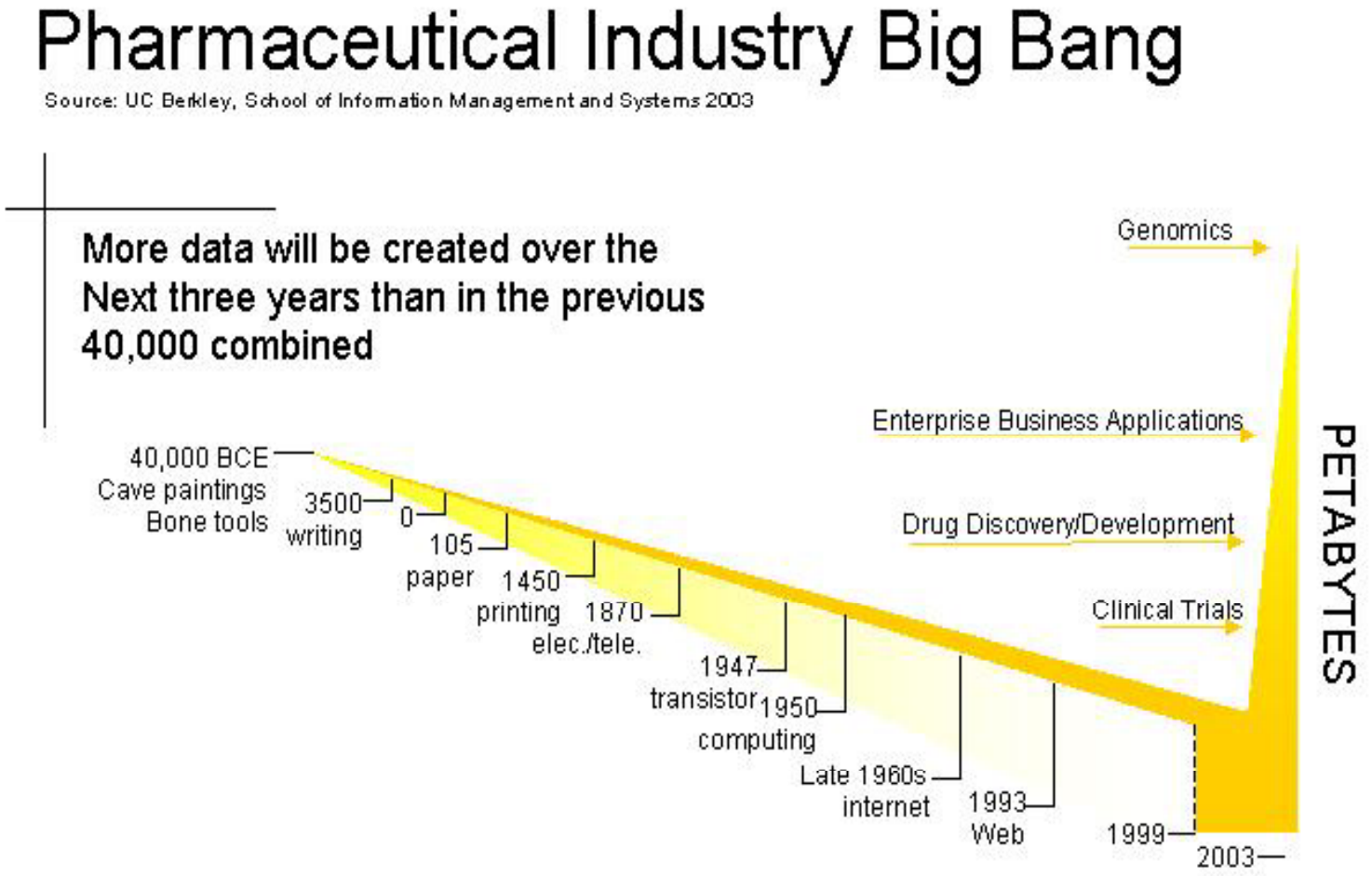
**But Big Companies are beginning to like Big Molecules**
**Gino Martini**

# The Human Genome Promise

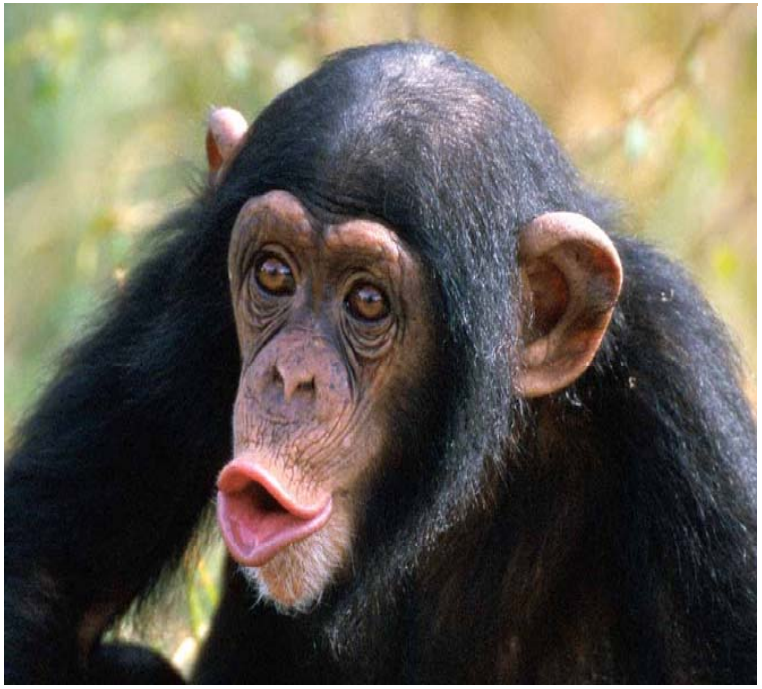


# Large Data Sets Will Be Pervasive In Healthcare



# But is that Simple?
## Whats the difference?



To some of my GSK colleagues, may be there is no difference

Genetically, there is 99.4% similarity!

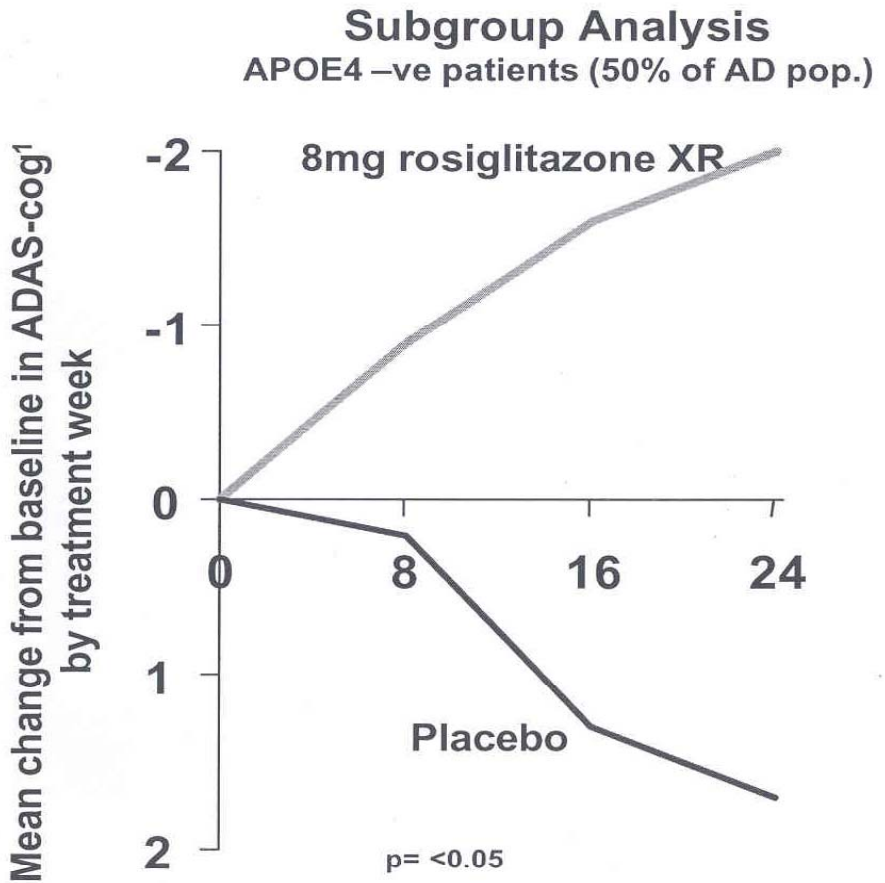
# We are ALL Different After ALL

The right treatment for the right person at the right time,
At the right cost for the right outcome

# Understanding the Human Genome

- New advances have allowed us:
  - To spot the disease earlier
  - To spot the chances of **you** getting the disease earlier
  - Realising the differences in patient populations
    - spotting who will respond to drugs or treatments from those who will not respond & finding new treatments from our drugs

# The Drug Maker's Roulette Of (missed) Fortune!




- Avandia although used for Diabetes has shown promising responses for Alzheimer's Disease
  - But only effective in a sub-group (50%)

# No More Magic Bullets

Polypharmacy is the key

# The Future Is Bright

In coming decades we can expect:

- Increased predictability of risks of disease
  - (Lots of research still to be done)

There will be major advances in:

- Immunology
- Predictive genetics
- "High throughput diagnostics"

- **The aim is treat people before they fall sick!**
- **Personalising our Medicines may be the SCRIPT for both Big Pharma & The Patient!**

**BETTER THERAPIES**
**BETTER COST CONTROLS**

# Integrated Healthcare – Examples of Work in Progress, The European Union

- The European Union has a program in place for *e-Health* for **citizen-centred health systems.**
- By 2010 it is estimated that the “e-Health Industry” in Europe will account for 5% of the total health budget with a turnover of some $12 billion.
- Telemedicine is already delivering benefits through tele-consultations (second opinion), telemonitoring (wearable or implanted monitoring devices) and telecare (first line advice or distance triage)

# Integrated Healthcare – Towards the Future

- The realisation of all of the projects underway today is that there needs to be an underpinning infrastructure and systems which will not only support what is there today but which can also provide the flexibility to include new systems and methods as they emerge tomorrow.


**Personal Health Recorder**

Imagine storing and carrying
Your health history in this
eMaxHealth Flash Driver for
emergency & personal needs.

**Buy for** $35.00

# But how do you personalise this!?

**This is the reality – polypharmacy & drug combinations**


- **C**

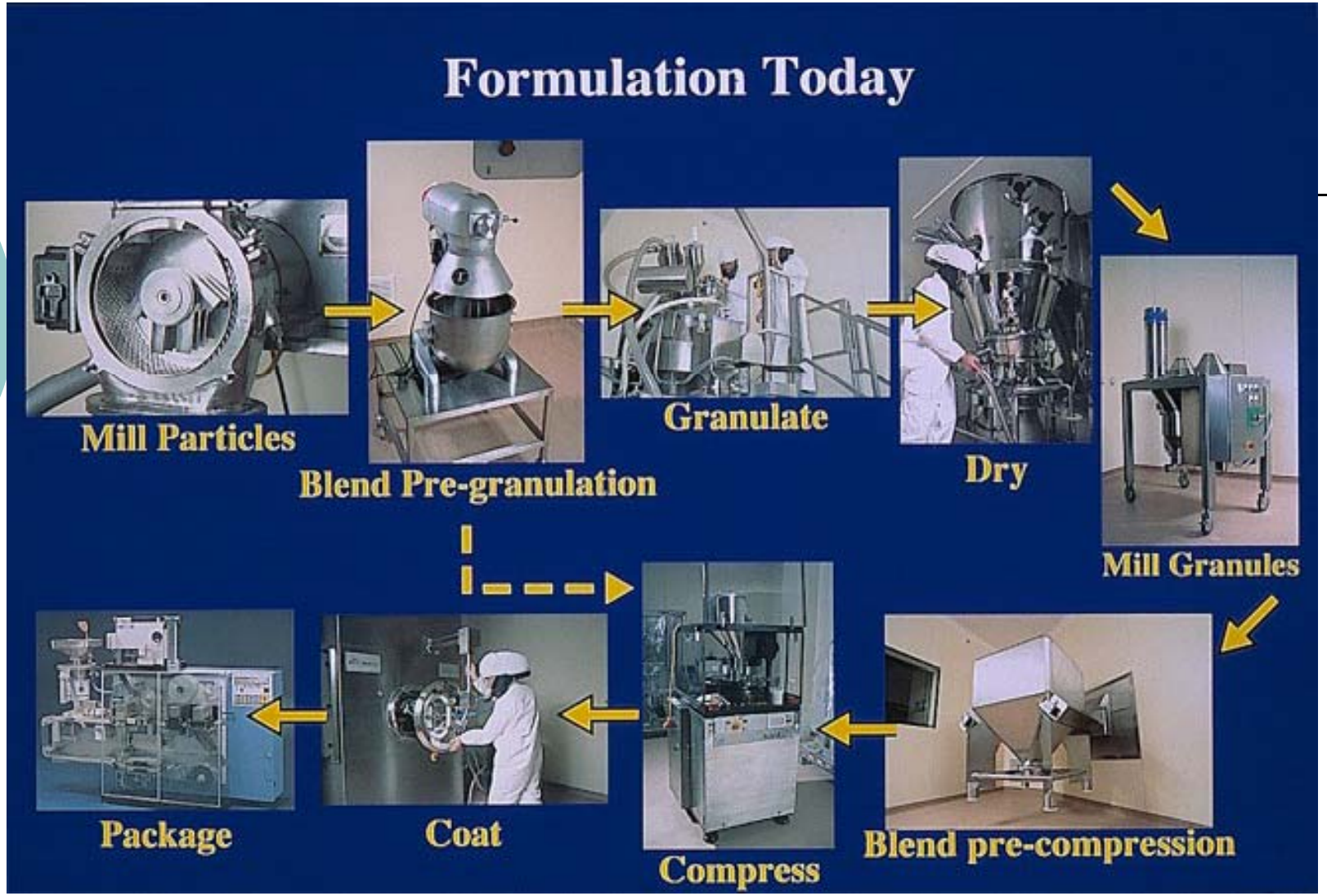
# Key Points to Summarise

Customized/Individualized medicines will require patients undergoing combination drug therapy i.e. more then one active drug product needs to be taken

- Medical advances are pushing towards targeted therapy

- Polypharmacy and poor patient compliance will be a major barrier to personalised medicine (Sir David Weatherall)
  - Non-compliance is estimated to range from 10 to 90% (depending on drug)
  - Drive towards the use of the terms ‘concordance’ and ‘adherence’

- The drive is to make every possible product/combination for all patients!




Capital Intensive, Heavily Regulated, Not changed for 150 years

# Key Points to Summarise!

Product Development & Manufacturing is a complex process

- Includes many steps and intermediate unit processes
- Has to cater for many variables
  - drug substance itself (API changes)
  - biological/clinical variables (often impacts dose)
  - manufacturing volumes & scale of development
    - accommodate large & small markets around the globe
  - heavily regulated process (lack of flexibility)
    - Changes are discouraged
  - failures!
    - 1 in 10,000 make it, 1 in 3 recover costs

⇒ Drives the tendency for mass standardisation

**Cannot make every strength!**

# Polypharmacy Strategies (historic approvals)

***patient needs using a variety of fixed dose combination is precedented.***

**Exemplary Launches of Combination Strategies**

1983 1985 1987 1989 1991 1993 1995 1997 1999 2001 2003 2005

- ***Self-Protecting Antibiotic***
- ***One Pill for Two Pathways***
- ***One Pill to Beat Mutations***
- ***Self-Correcting Pill***
- ***Self-Correcting Packages***
- ***One Pill for Two Conditions***

Augmentin®

Capozide® Vaseretic®

Hyzaar®

Glucovance®

Advair®

Vytorin®

Combivir®

Trizivir®

Truvada®

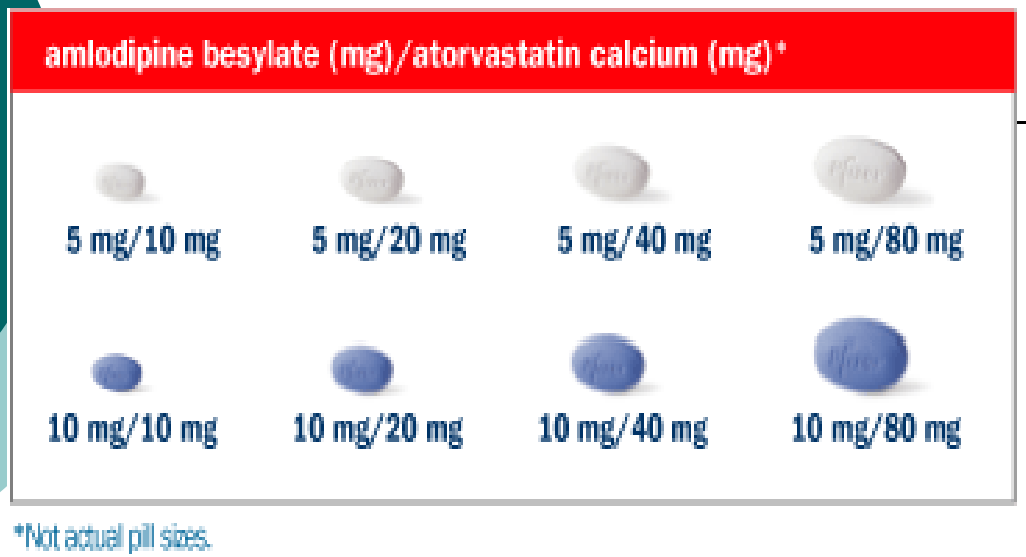
Arthrotec®

NapraPAC®

Symbyax® Caduet®

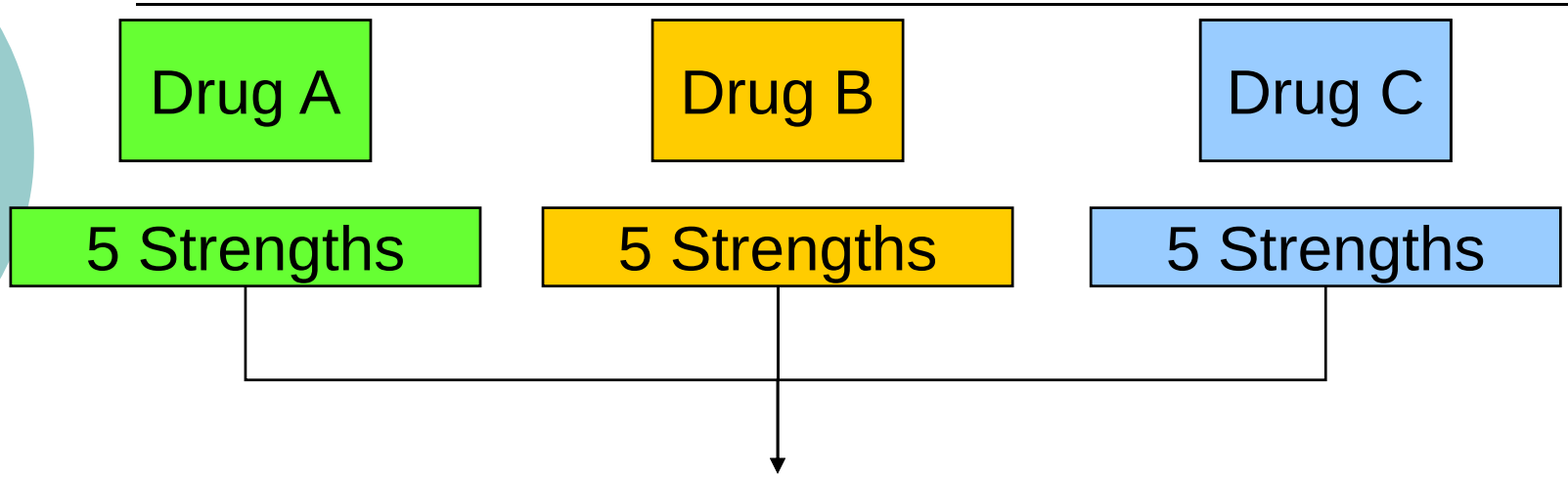
GPIE EIPG

# The Current Paradigm




- Conventionally, most combination products are delivered as either compressed mixtures or as compressed layers.
  - Both approaches are fixed dose
  - Both approaches rely upon good stability and compatibility.
  - Both approaches require a high number of permutations.

# The Problem with Fixed Dose Combinations




ABC = CBA same combination, different permutation

3 Drugs x 5 Strengths = 15 variants

Combinations = 5x5x5

= 125

# Combination products

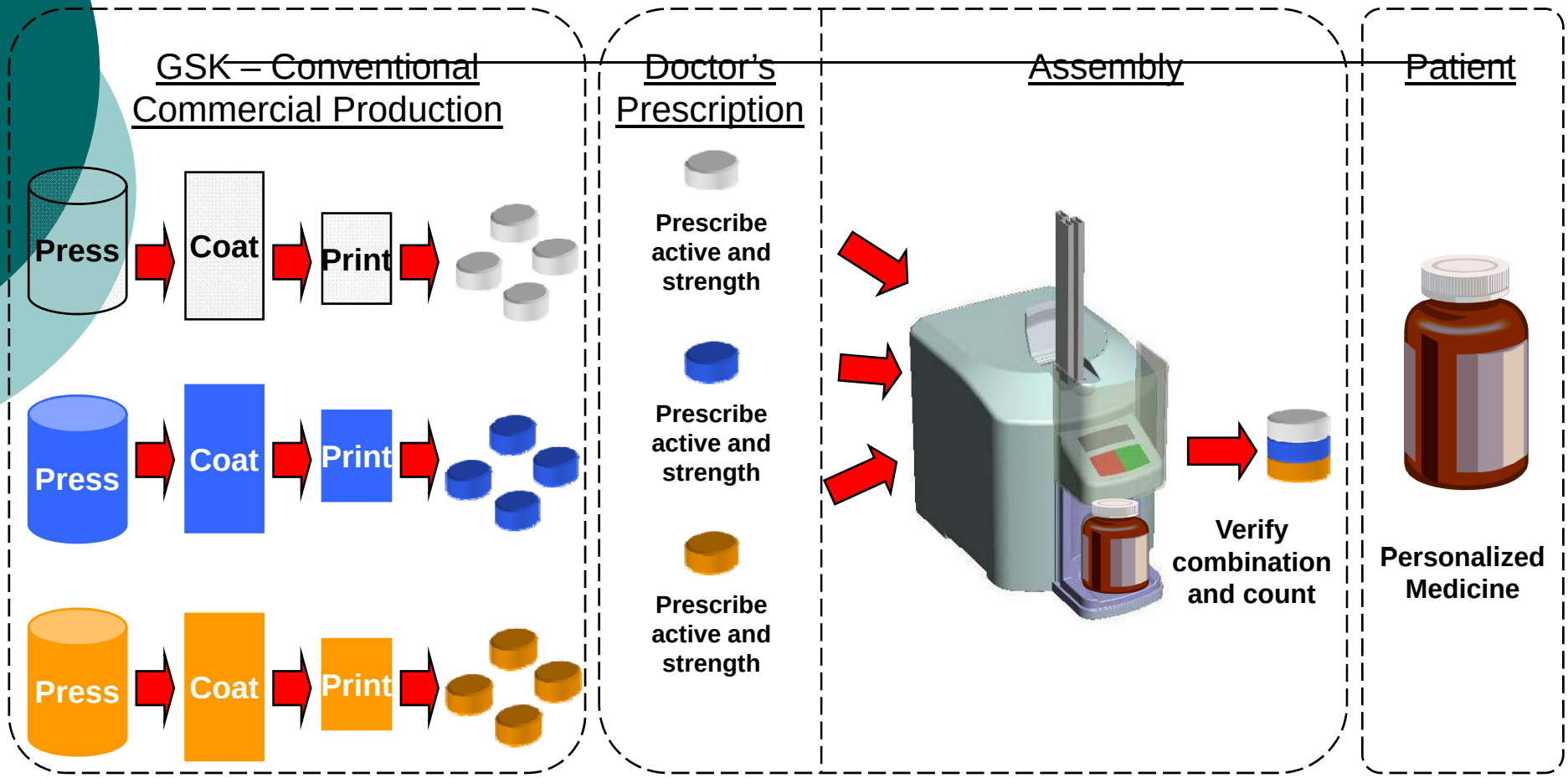
**"…... But doctors often avoid prescribing combination drugs because they come in a limited number of dosage choices, making it difficult to customize drug regimens or solve problems patients experience on a single pill."** ***The Wall Street Journal 29 Jan 2004 (Abstract)***

What are the solutions?

# Could this be the New Paradigm Scenario

- Do we see a return to the compounding Pharmacist?
  - Dispensing to an individual needs
  - Could complement prescribing pharmacists skill-sets?
  - Real pharmacy
- **0.019%** of prescriptions are extemporaneously prepared in a dispensary (THS,2006)
  - pricing vs time constraints
  - liability concerns
  - ‘mopped up’ by the ‘specials’ pharmaceuticals companies

# Could We Do this?



# Pharmacy Device

# Science Needs You!

From The Times

February 20, 2007

**Drugs industry short of UK graduates**

Robin Pagnamenta, Healthcare Industries Correspondent

GlaxoSmithKline has given warning that a lack of UK science graduates is forcing Britain's largest drugs company to recruit from overseas to fill key research posts.