# Combining Scientific and Medical Innovation into the progressive translation of cell therapies

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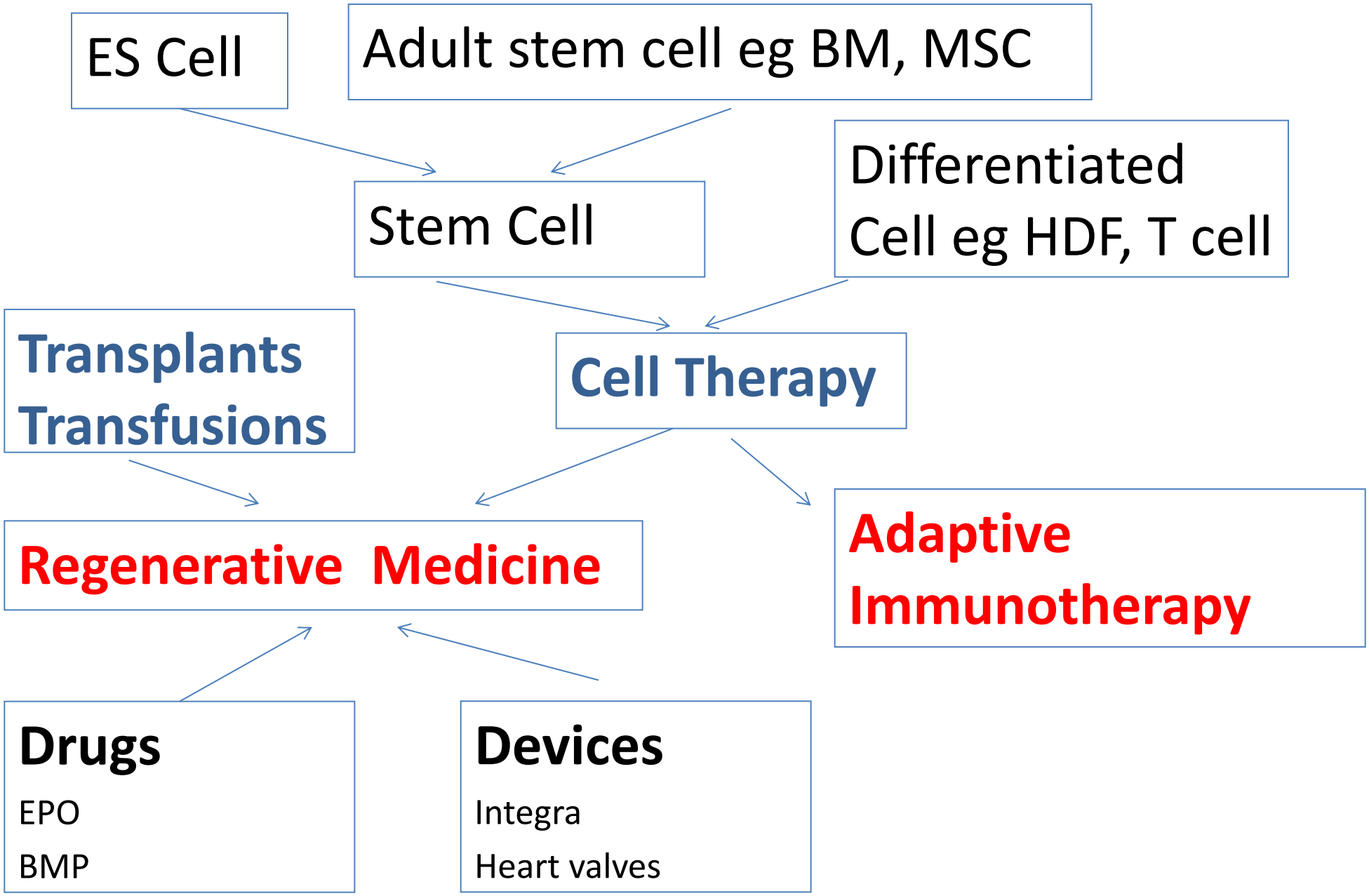

ES Cell
Adult stem cell eg BM, MSC
Stem Cell
Differentiated Cell eg HDF, T cell
Transplants Transfusions
Cell Therapy
Regenerative Medicine
Adaptive Immunotherapy
Drugs
EPO
BMP
Devices
Integra
Heart valves

# Scientific Innovation

Various permissions can take years, . Protocol “best guesses” changes can take months. Trials are costed at “commercial rate”. Regulators decide on efficacy

Product Develop-ment

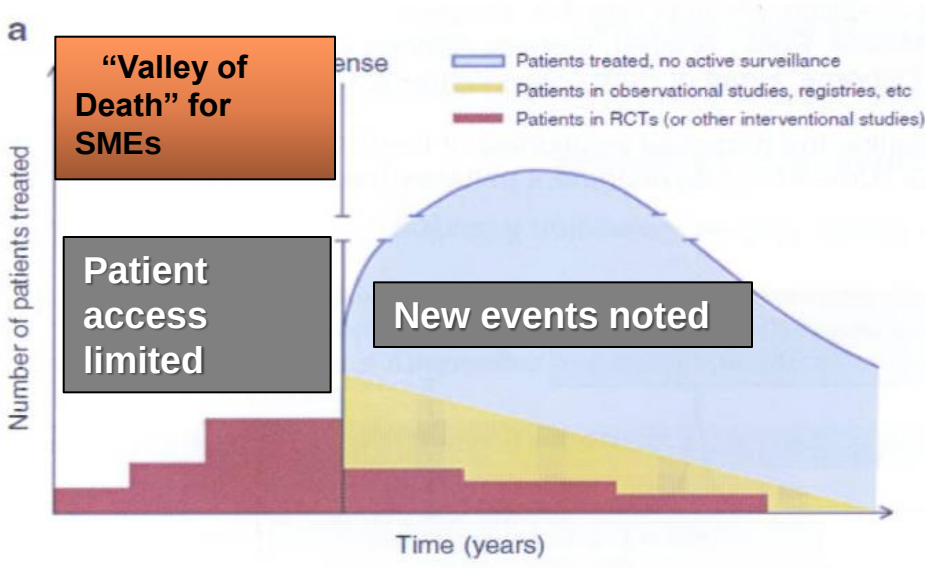
Pre-Clinical Experimen-tation

Clinical Trials

Product Approval

Marketing and Broad Clinical Application

**Industry Sponsor driven**



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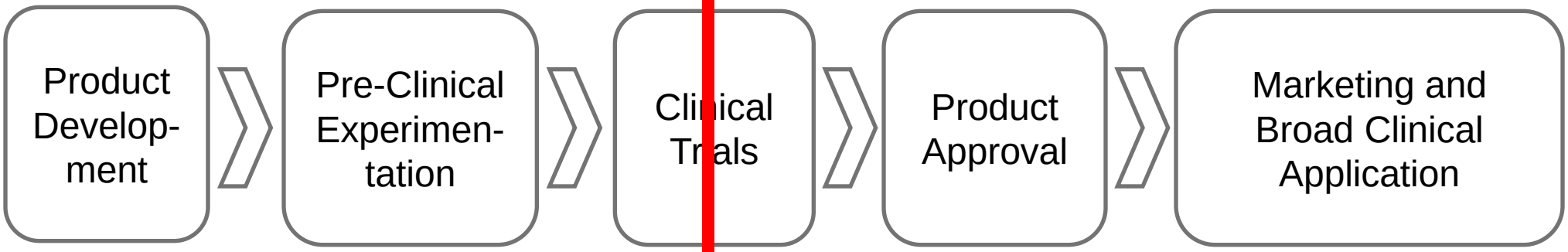
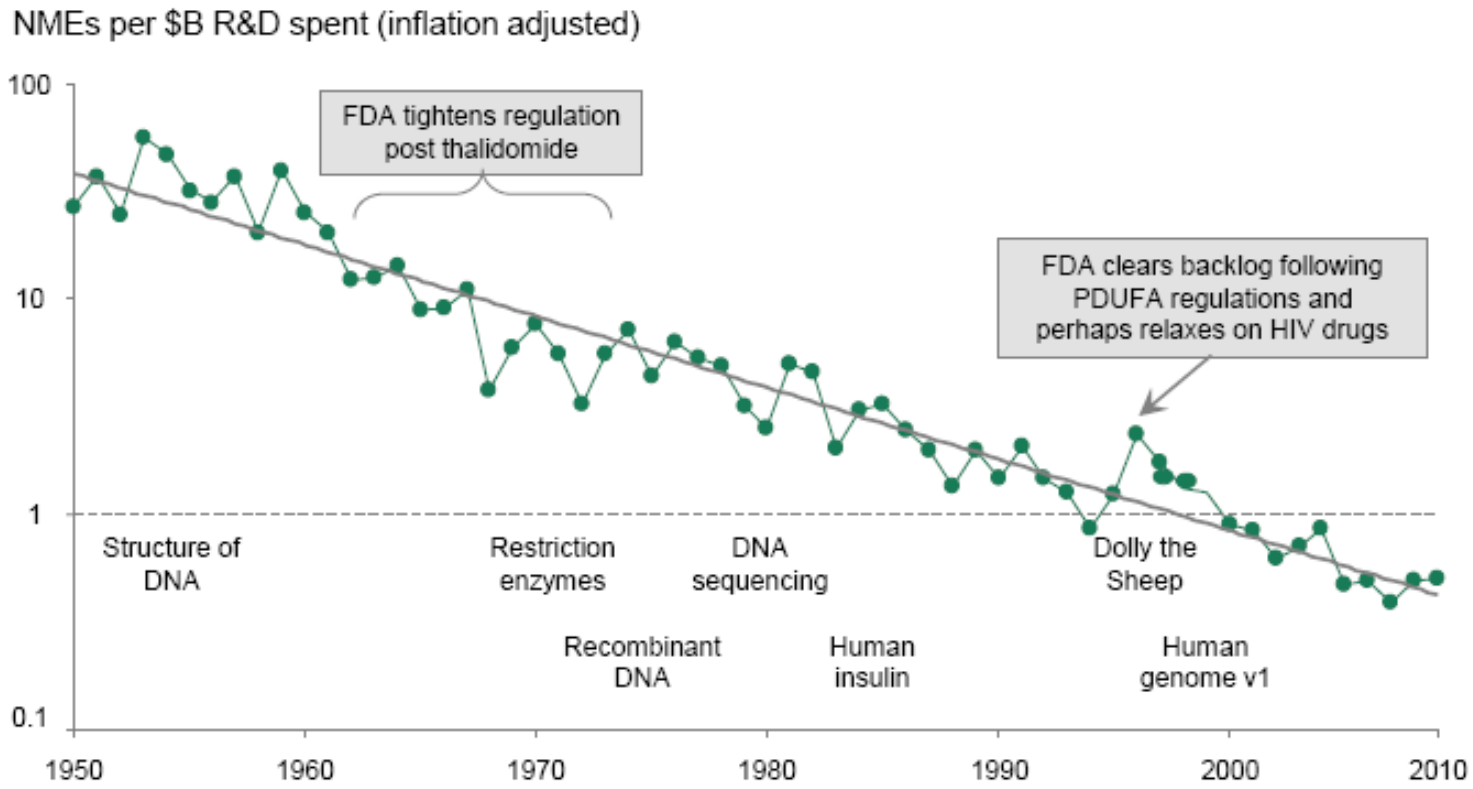



**Industry Sponsor driven**

- Intercytex/Cyzact
- Shire/Dermagraft
- Athersys/Multistem

- Ulcerative Colitis
- Randomised, double blind placebo controlled
- 106 patients treated in total with one application
- US, Canada, Germany, Sweden, Hungary, Slovakia, Italy
- At 4 weeks the proportion of responders in multistem cohort significantly higher than placebo but benefits offset by declines in minority subgroup
- “These results tell us that single administration is not sufficient we anticipate additional data from patients who have received additional treatments which may provide more insight”
- Share price dropped 60% in a day >$100M drop in valuation

# R&D productivity is on the decline




Note: R&D costs are estimated from PhRMA annual survey 2009; NMEs are the total number of small molecule and biologic approvals by the FDA
Source: Bernstein Research "The Long View – R&D Productivity" (September 30, 2010)

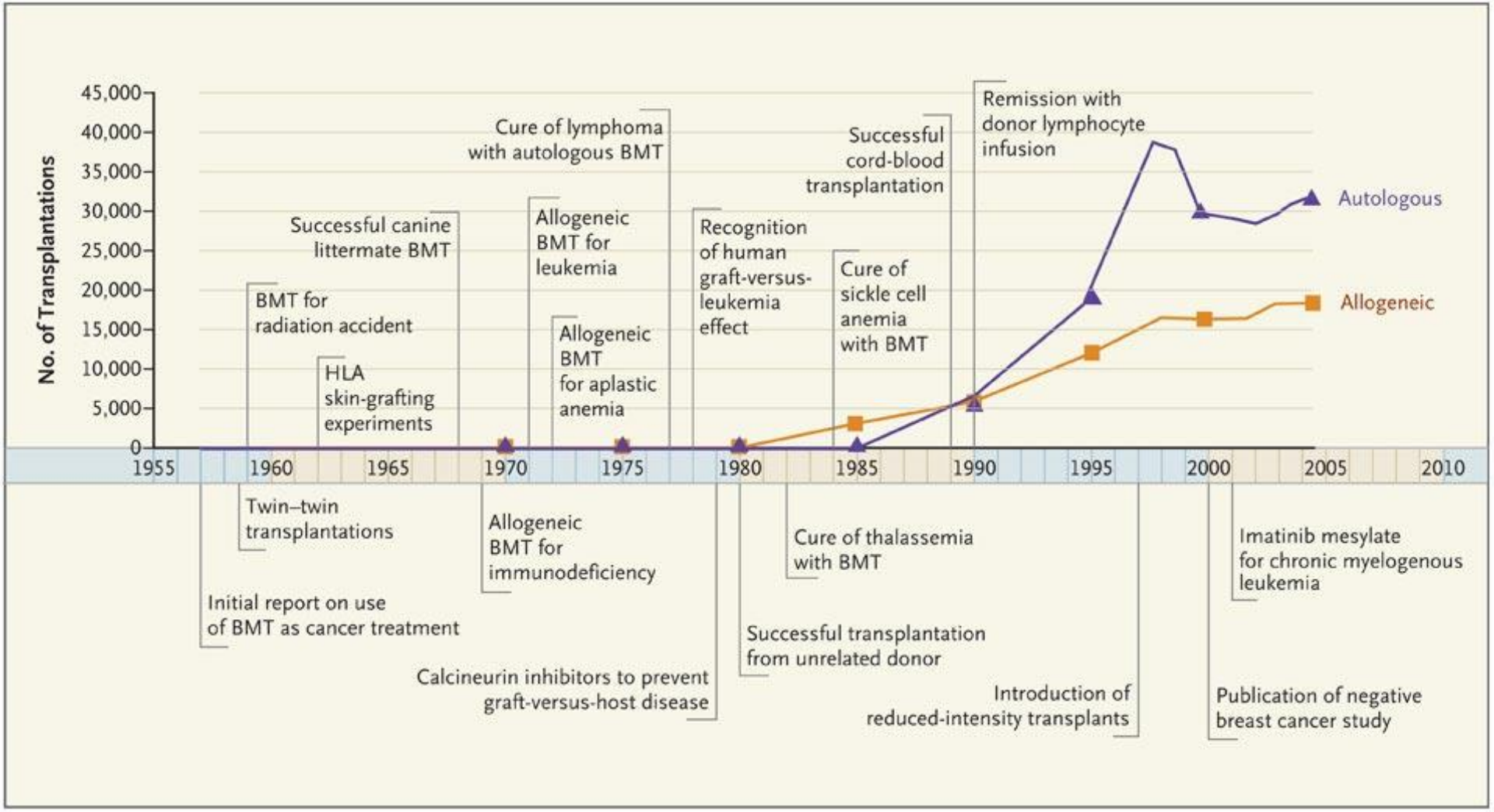
# The winners end up paying for the system

- Sovaldi by Gilead for Hepatitis C
- Effectively cures >90% of time with less side effect
- In US, patients charged $84,000 for 12 week treatment
- Sales $2.3Bn in the first quarter of 2014
- Share price increased 83%, market cap increase $58Bn
- In Germany, patients charged $66,000
- Egypt, patients charged $900
- 80 group campaign in US to pressure cost reduction

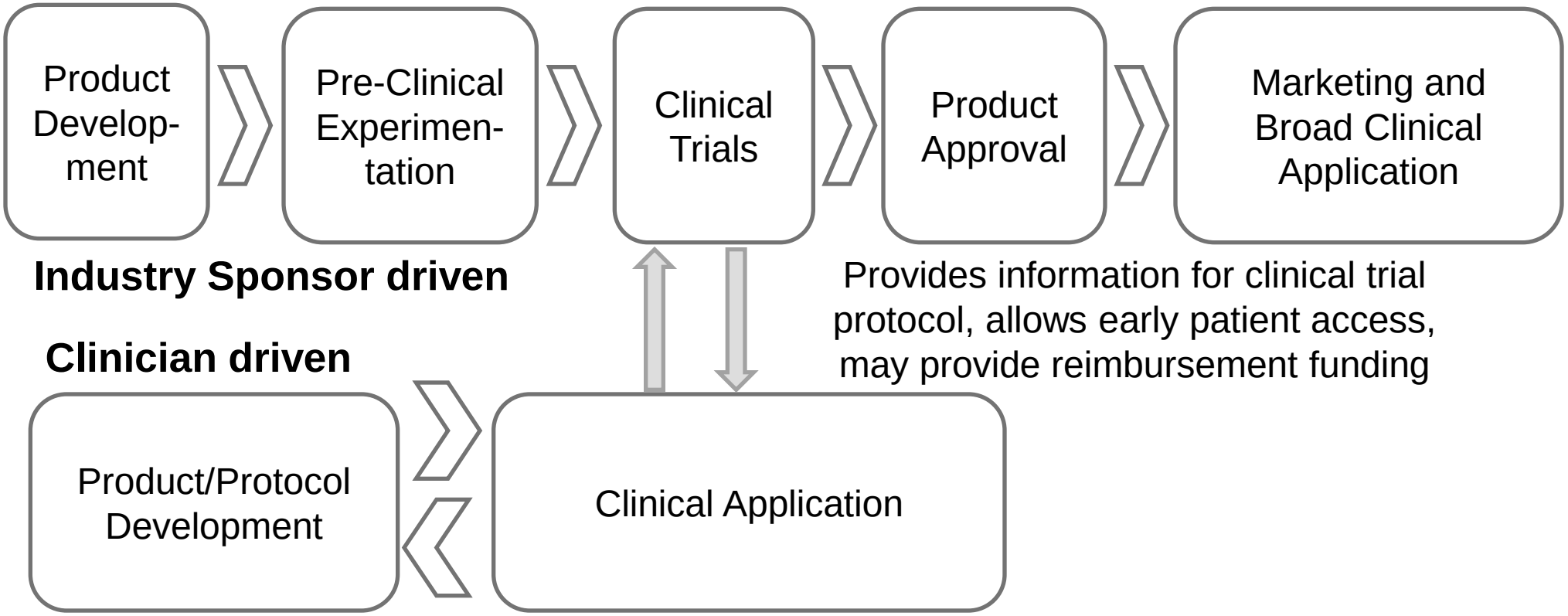
# But reimbursement can change

- Medicare/Medicaid reduce reimbursement for Regenerative Medicine wound care treatments Apligraf and Dermagraft
- Shire who had bought Dermagraft for $750M “sold” it for $300M milestone payments to Ortganogenesis
- Organogenesis close Dermagraft manufacturing facility and lay off many of their own staff including all of R+D
- Sanofi sells RM business purchased through Genzyme acquisition to Aastrom for 10% of 2013 sales

# Scientific Innovation vs Medical Innovation



# Progressive Translation, combining best of both



# MHRA Report of the Expert Group on innovation in the regulation of healthcare (25th Sept 2013)

Intercytex

"The expert group considered in relation to quality, safety and efficacy aspects, the concept of adaptive licensing would need to relate to a more proactive use of existing flexibilities in European law……The development of new or revised legislation requires a lengthy process"

…there was less awareness of these flexibilities among all UK companies that was commonly assumed… It was recognised that innovative products or technologies are often developed by academics or SMEs who have little or no regulatory affairs expertise. However, the Expert Group considered more could be done to communicate flexibilities to industry.

# Unlicensed Advanced Therapy Medicinal Products

2 mechanisms to enable the use of unlicensed ATMPs:

- Specials (Directive 2001/83/EC – article 5(1))
- Hospital exemption (Regulation No. 1394/2007)

Both are regulated at a National level (by MHRA in the UK)

# Unlicensed Advanced Therapy Medicinal Products

## Specials

- Supplied to fulfil a special need test  i.e. no equivalent licensed medicinal product available.
- Products are manufactured/prescribed by doctor, dentist or other supplementary prescriber. The administration and specification of the product is the prescribers responsibility.
- No stipulation on where i.e. hospital/private clinic, the products can be administered.
- Specials can be imported into, and manufactured in, the UK; they can also be imported out of the UK

# Unlicensed Advanced Therapy Medicinal Products

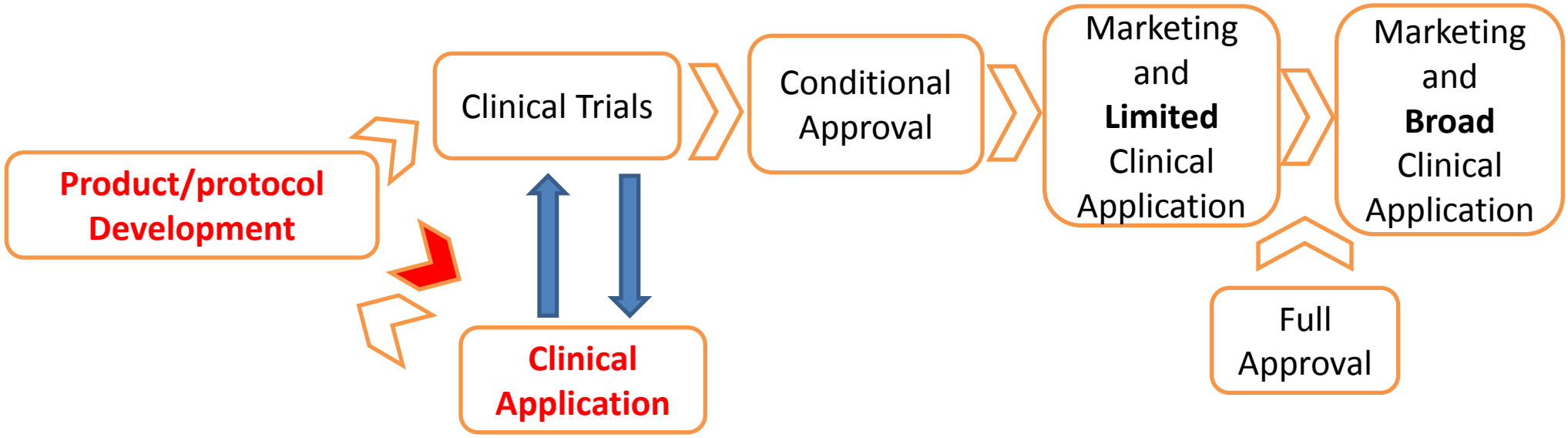
## Hospital Exemption

- Can only be commissioned by a medical practitioner.
- Must be custom made to meet an individual prescription and preparation must be on a “non- routine basis”.
- Must be used in a hospital.
- Must be prepared and used in the same member state i.e. no import/export permitted.

# Progressive Translation

- Utilise existing international regulatory flexibilities to gain early patient access pre full marketing license.  This will inform later trials (protocol, follow-up times, efficacy for SAP, patient numbers). This leads to eventual full licensing and broader patient access
- eg
  - UK Specials
  - EU Hospital Exemptions, Conditional Licensing
  - US Breakthrough Therapies
  - Japan?

# Progressive Translation
# Medical Innovation combined with Scientific Innovation



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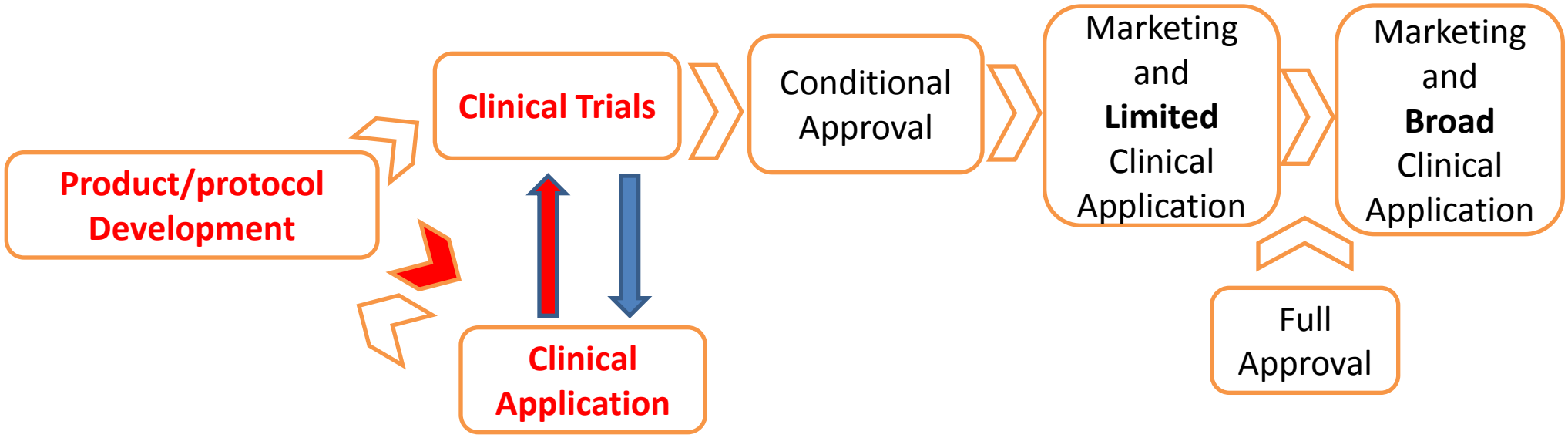

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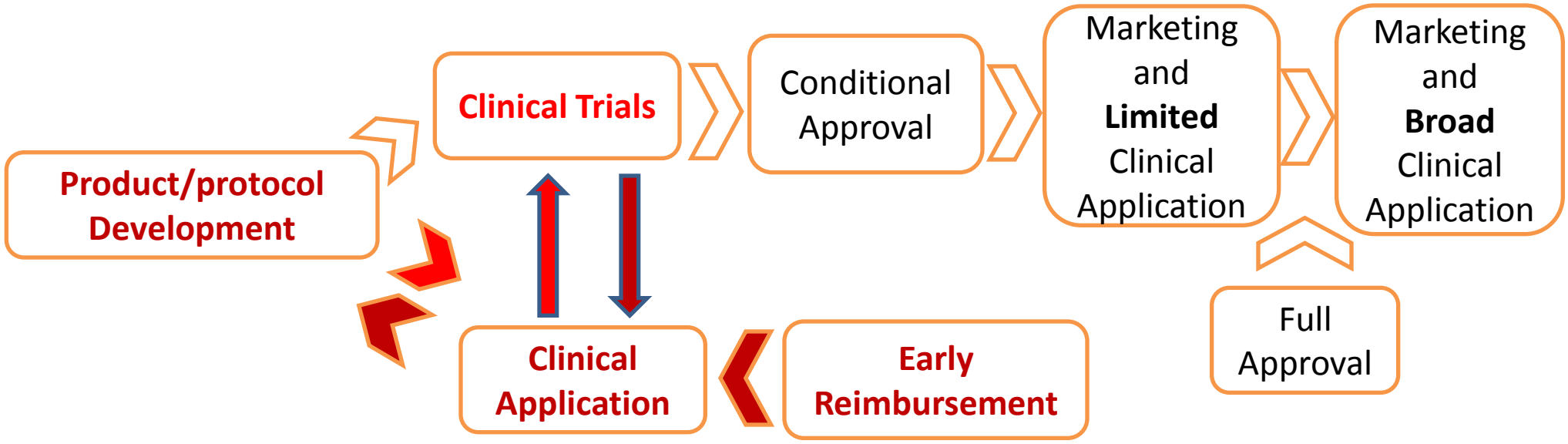

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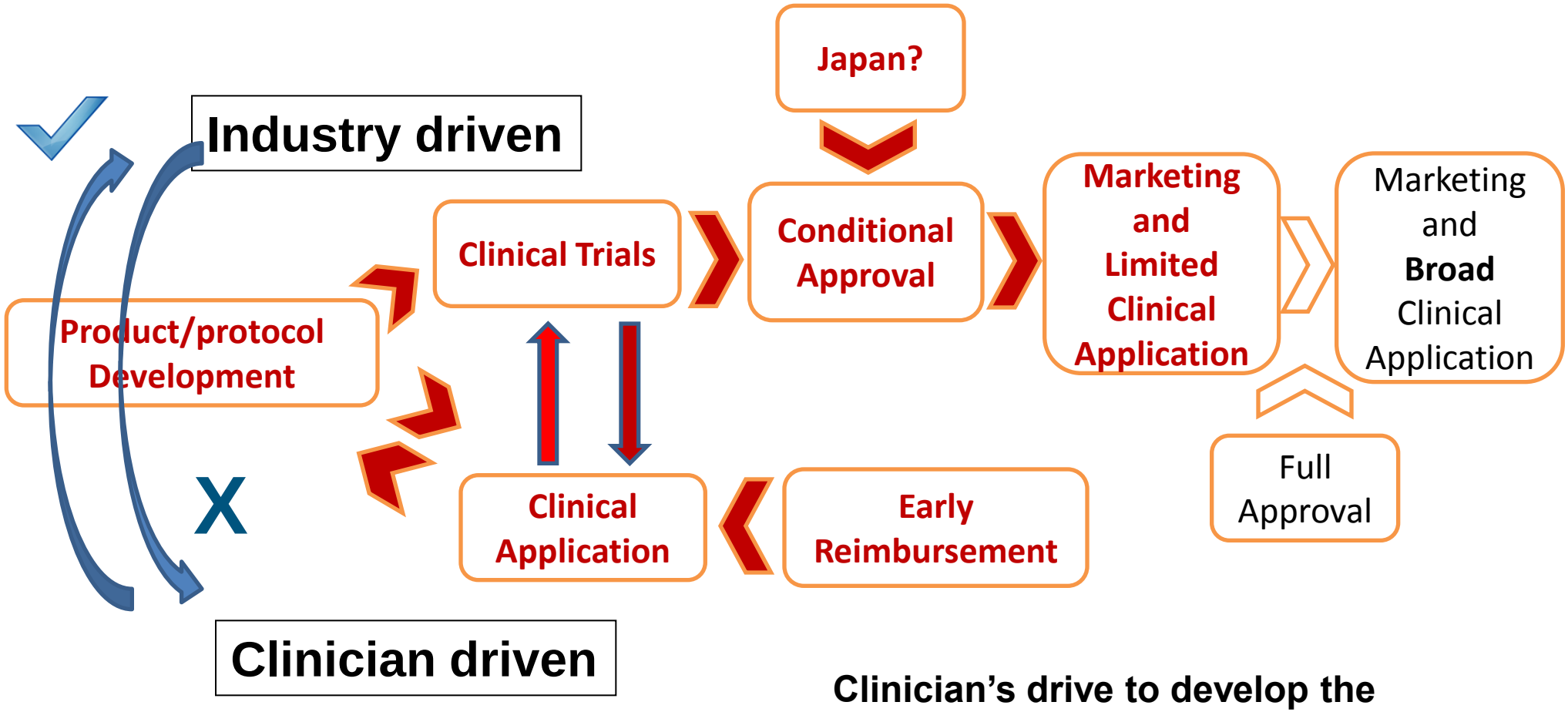


**Clinician's drive to develop the product/protocol is critical**

# Questions

- What might the future look like if nothing is changed?
- How can the practice of medicine be best used to develop treatment protocol and inform clinical studies?
- How can clinician/industry interface be used in order to inform product development and clinical application within current legislative framework?
- How can patients be involved in this development process?
- What sources are available for progressive reimbursement. How could pricing be determined? How could risk sharing be used?
- Managing hype, ethics, conflicts of interest, social perceptions and regulatory change?
- Threats and opportunities to UK landscape?

# Thankyou

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