



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Adaptive Licensing: a useful approach for drug licensing in the EU?

EMA, London, March 2012  
Hans-Georg Eichler





## The EMA Mission...

is to foster scientific excellence, for the benefit of public and animal health.

### Guiding principles

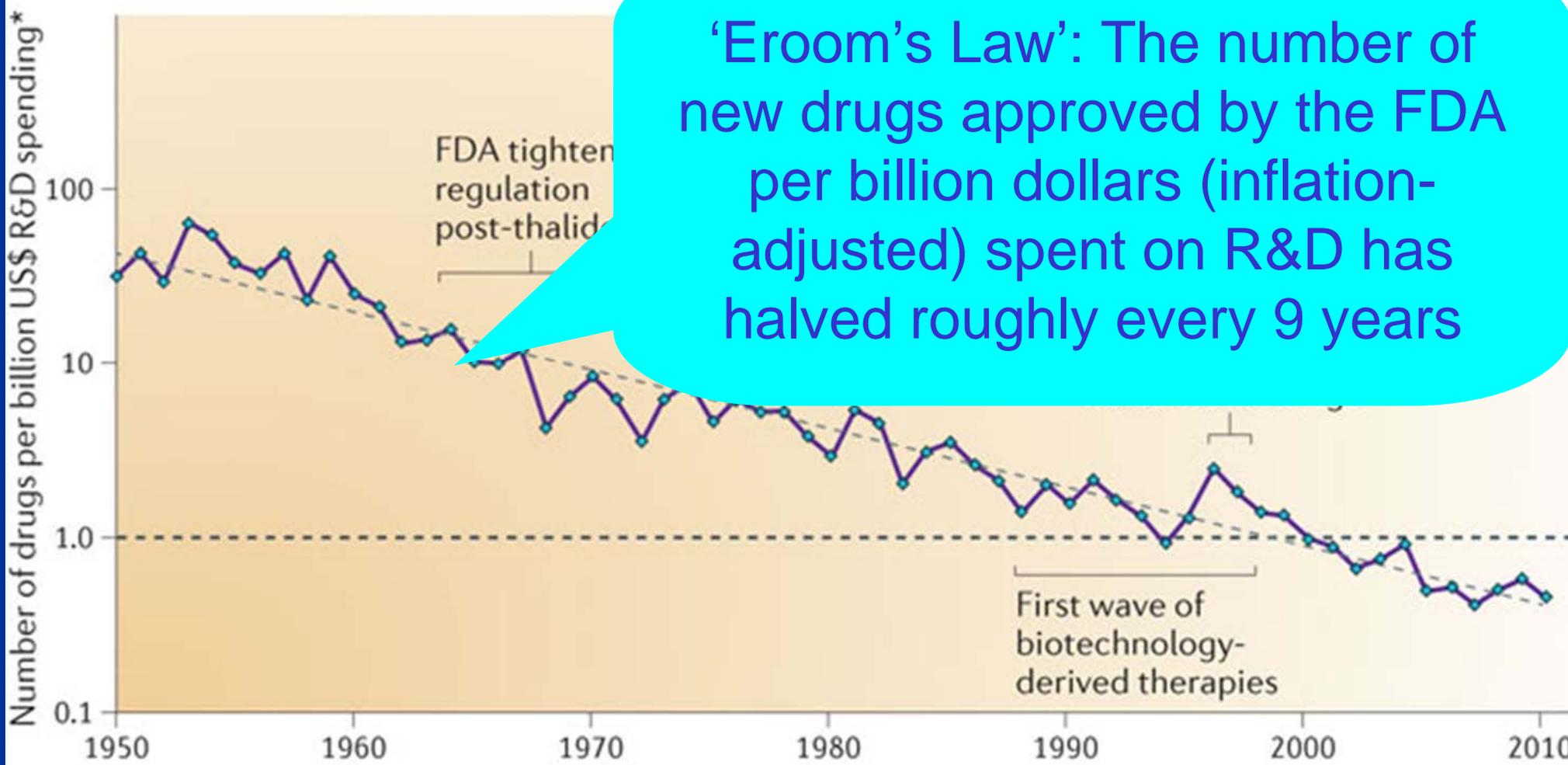
We are strongly committed to public and animal health.

We support research and innovation to stimulate the development of better medicines.

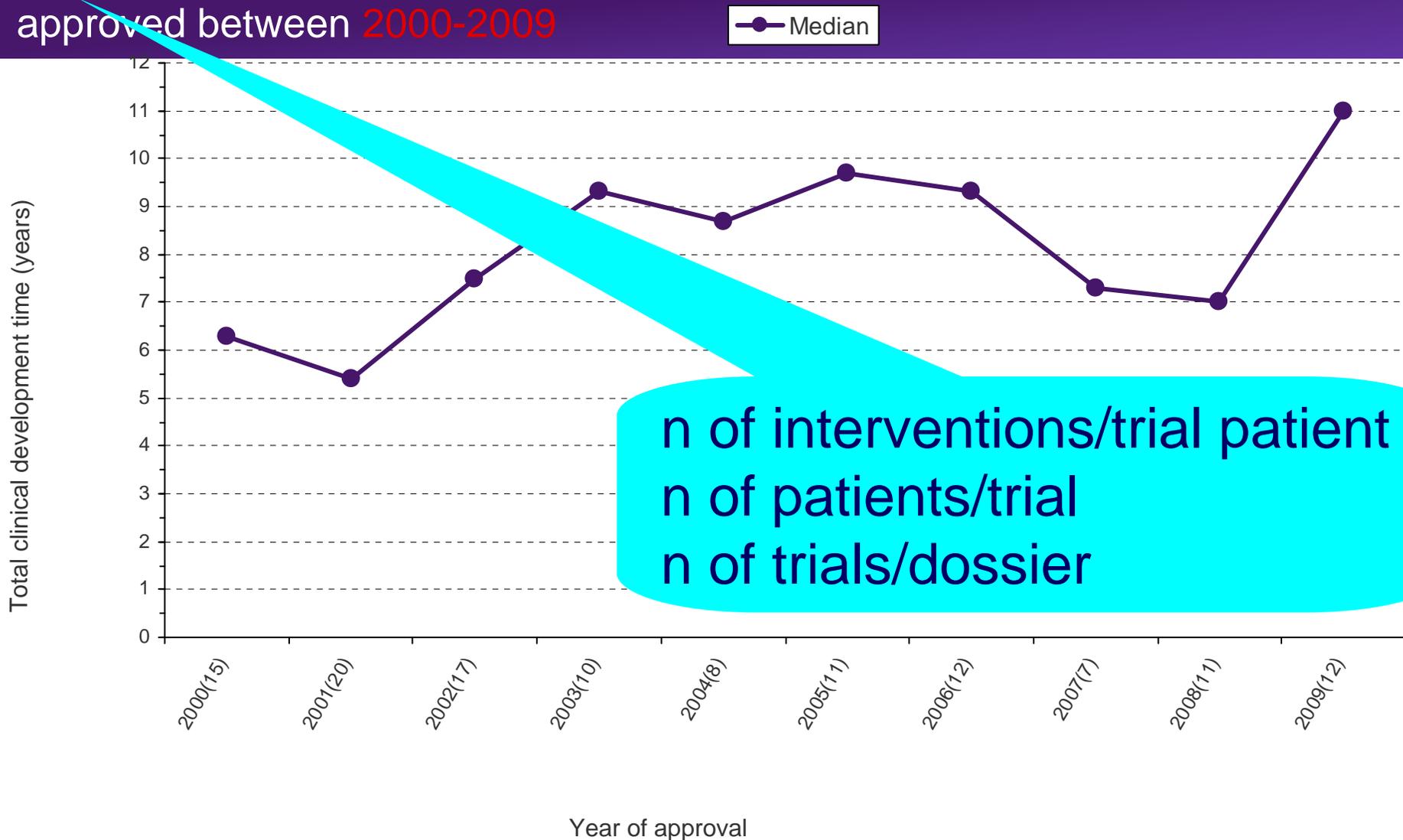
**Gatekeeper and Enabler**



a Overall trend in R&D efficiency (inflation-adjusted)

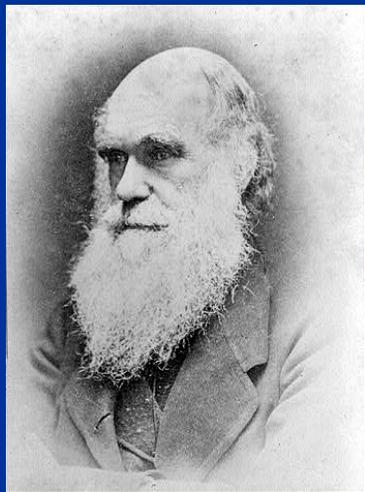


# Trend in actual clinical development time for new development projects approved between 2000-2009



Actual clinical development time is calculated for new development projects as the time between 'First human dose' (T-1-1) and 'First approval' (T-4-2). Data represent all new development projects that reached 'First approval' (T-4-2) between 2000-2009, where the start and end milestone dates for the interval are available. (n) = number of projects analysed in each year. This analysis is based on data from a consistent cohort of 17 companies participating each year between 2001 and 2010.





# Evolution of life

Mutation

Selection

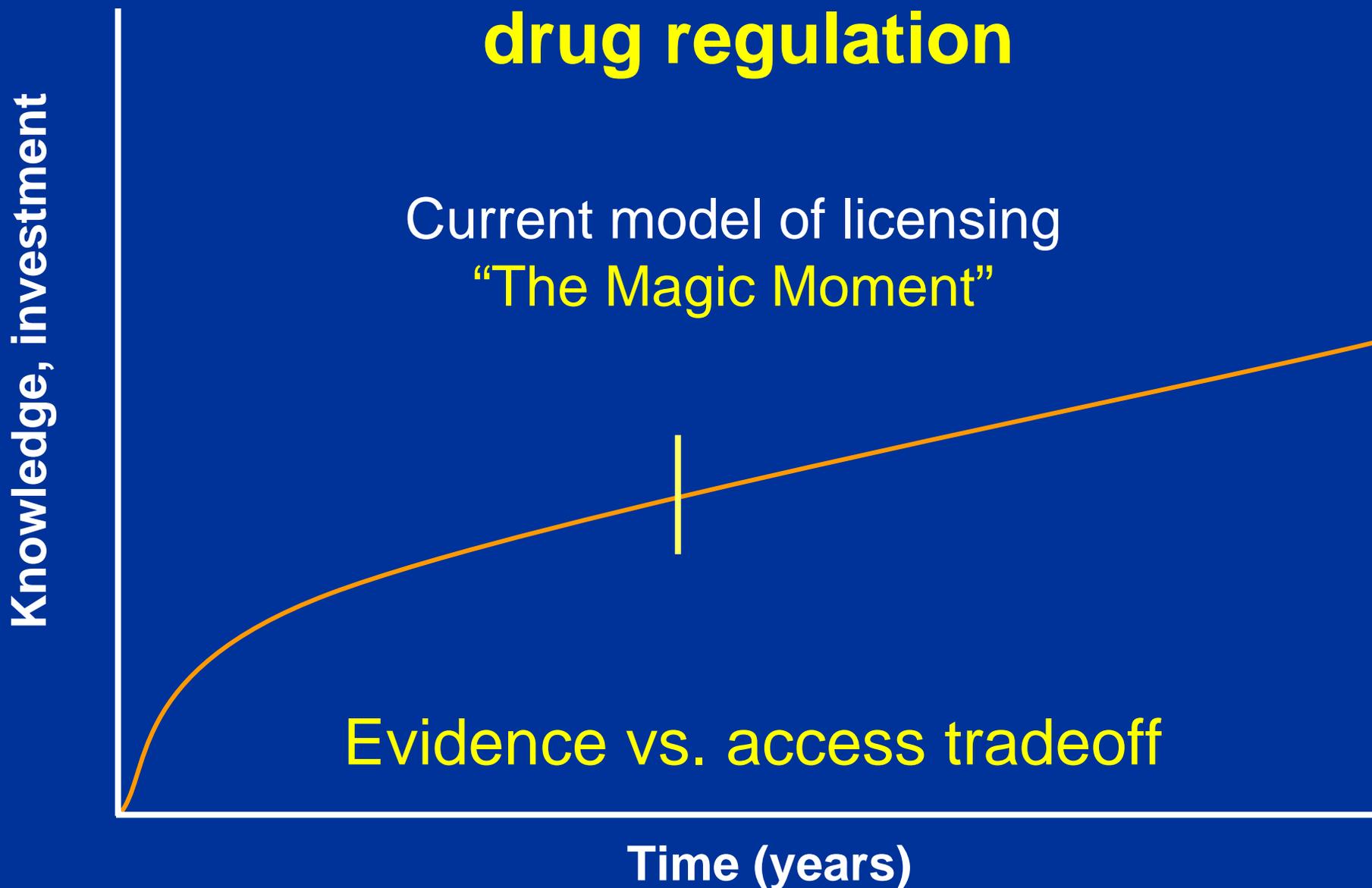
# Evolution of drug regulation

Catastrophe

Clamp Down



# The binary nature of drug regulation





## The regulator's dilemma

“...it has been said that the FDA has just two speeds of [drug] approval – too fast and too slow.”

Hamburg MA & Sharfstein JM. NEJM 360;24: 2493-5; 2009



## EMA Road map to 2015

[...] a key issue for regulators will be whether a more ‘staggered’ approval (or progressive licensing) concept should be envisaged for situations not covered by conditional marketing authorisations [...]

The Agency would like to launch a debate with all stakeholders on the appropriateness of introducing such a concept, including a consideration of appropriate incentives to support new medicines development.



## Different names, same ideas

- EMA: staggered approval
- FDA: progressive reduction of uncertainty
- Health Canada: progressive authorization
- HSA Singapore: test bed for adaptive regulation
- Payers (HTAi): managed entry
- MIT/NEWDIGS: adaptive licensing project



# “Precursors” to Adaptive Licensing

- Conditional Marketing Authorization
- New Pharmacovigilance legislation
- Risk Management Plans
- Periodic Safety Update Reports
- Five-year renewal of marketing authorization
- (Compassionate use programs)



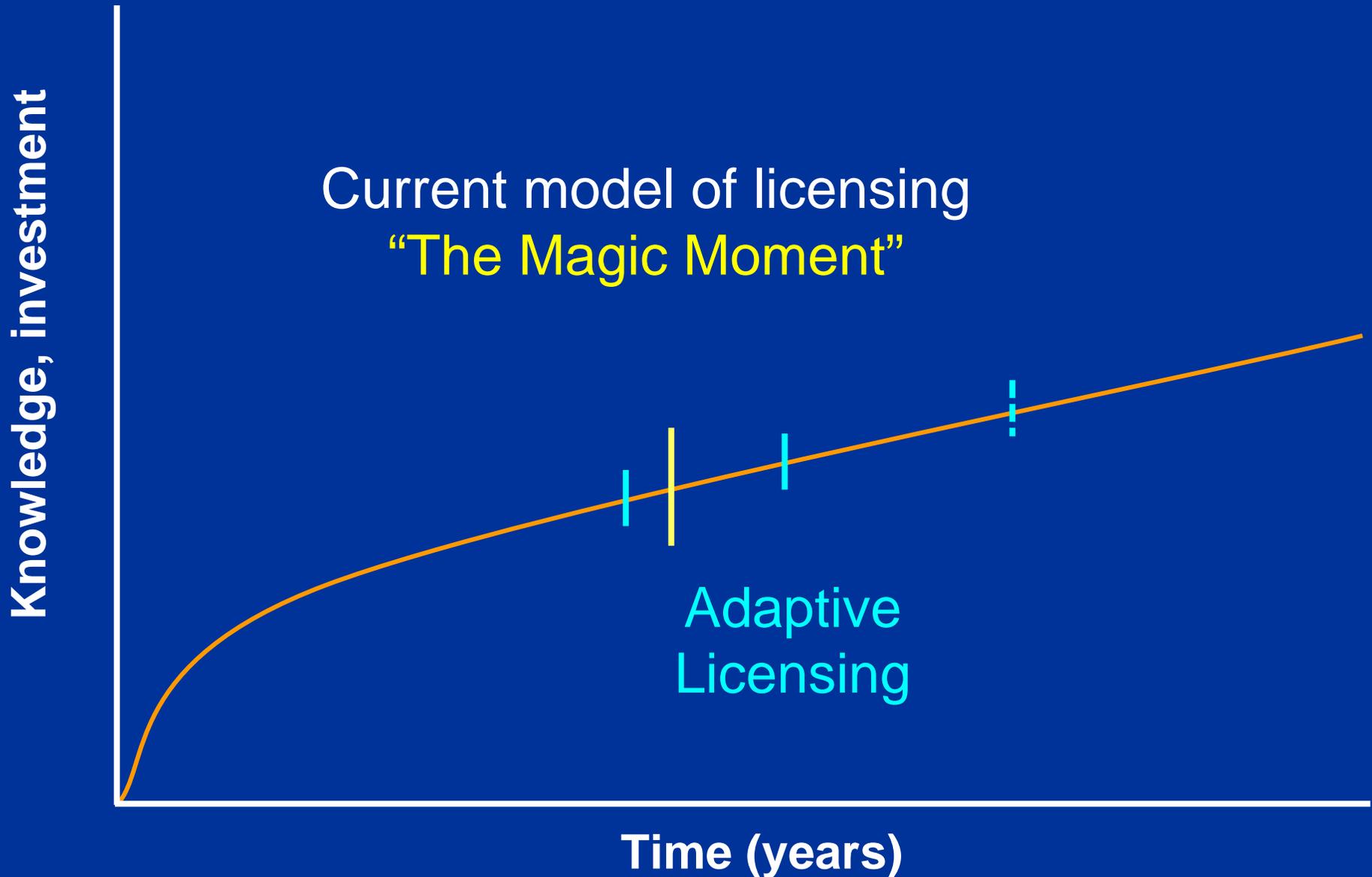
# Conditional Marketing Authorisation

	New Active Substances* Centrally approved	Of which Conditional Marketing Authorisations
2009	29	0
2010	17	4
2011	23	2
<b>Total</b>	<b>69</b>	<b>6 (= 8.7%)</b>

\* Definition as per EMA Annual Reports

Standard route to market is 'binary'

# A better model for evolution?





# Adaptive Licensing

AL is a prospectively planned, adaptive approach to regulation of drugs.

Through iterative phases of evidence gathering followed by regulatory evaluation and license adaptation,

AL seeks to maximize the positive impact of new drugs on public health

by balancing timely access for patients with the need to provide adequate evolving information on benefits and harms.



# Adaptive Licensing

AL builds on existing regulatory processes, including Conditional Authorization and existing PhV tools.

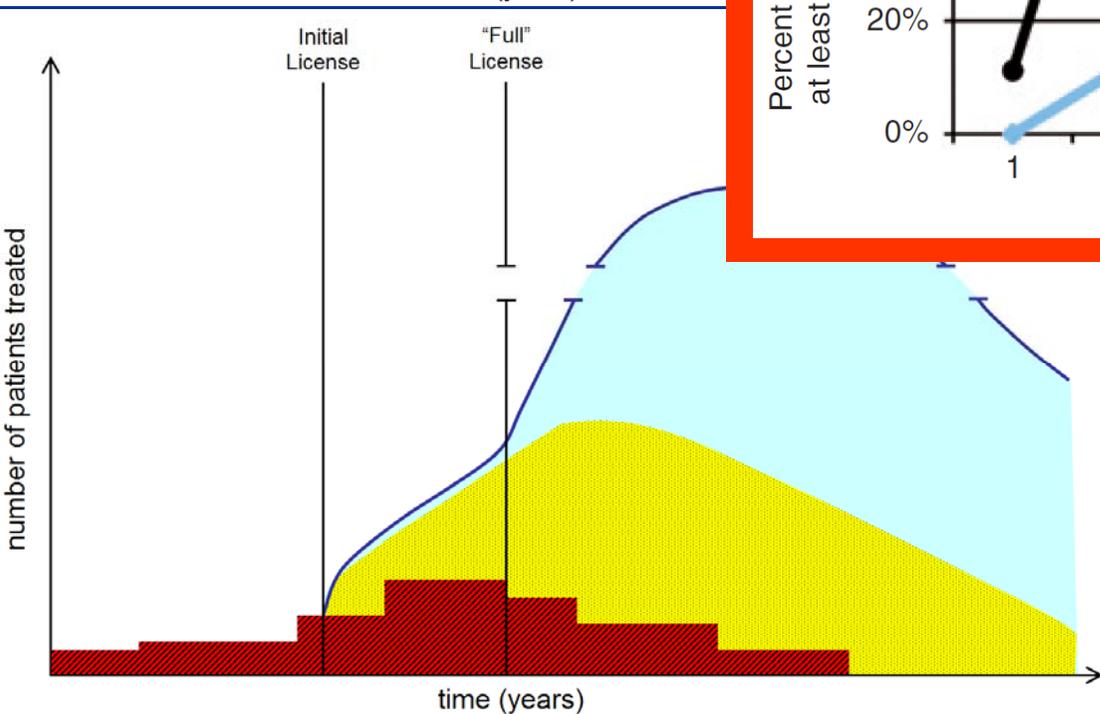
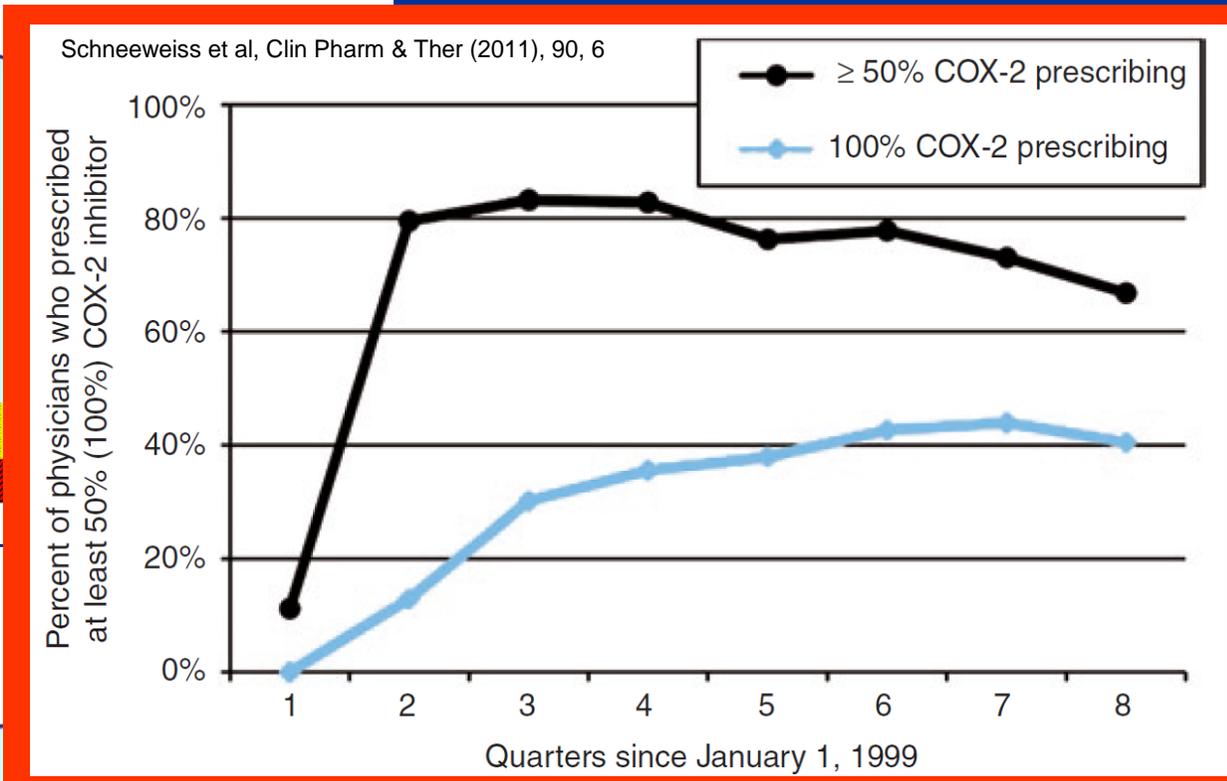
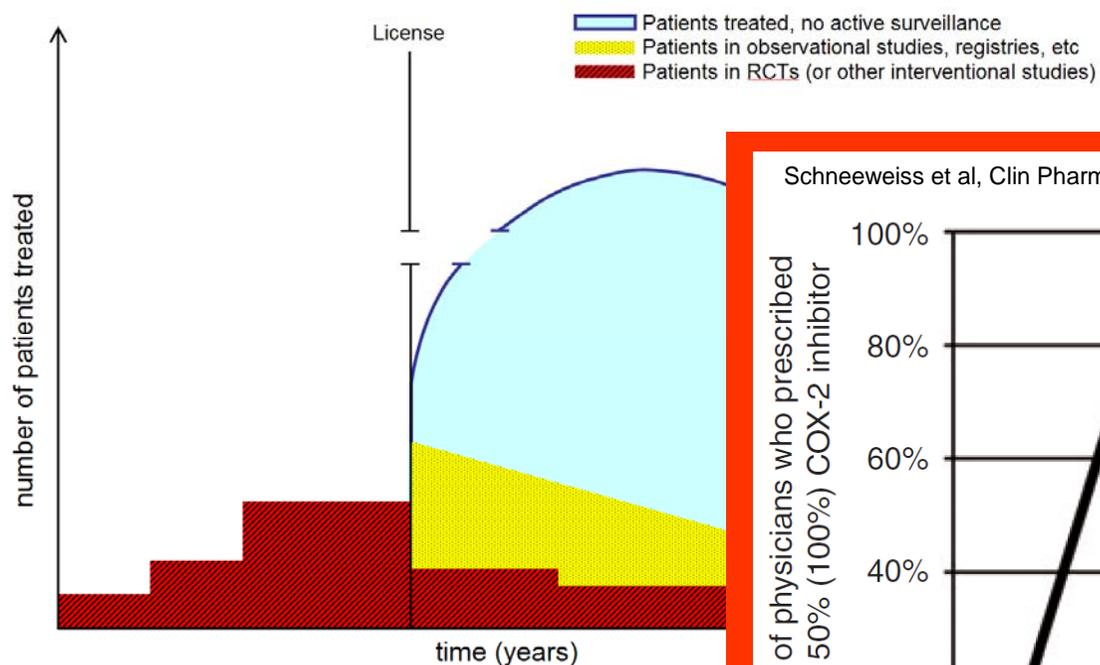
To achieve the full potential of AL, licensing decisions should ideally be aligned with coverage and prescribers' decisions.



# AL scenarios – “design factors”

## Incremental vs. transformative approaches

- broaden treatment-eligible population
- reduce uncertainty around endpoint
- reduce uncertainty around study design
- reduce statistical uncertainty
- enable new-new combo development
- ensure effectiveness
- address rare Adverse Events



treated patients grows more slowly, due to restrictions; patient experience is captured to contribute to real-world information



## Obstacles to Adaptive Licensing

- concerns over lowered standards
- how to communicate uncertainty?
- doable under current statute?
- getting commitment from industry to conduct “stage n+1 studies”?
- are follow-on studies doable after “loss of equipoise”?
- alignment between regulators and payers
- different reward structure required to incentivise drug development enterprise?
- ensuring appropriate prescriptions



## Addressing the obstacles; next steps?

- Address economic consequences for drug development sponsors - historical case studies
- Design pilots cases using current sponsor assets
- Address legal underpinnings of AL
- Explore opportunities for collaboration with payers
- Obtain buy-in from all ranks of regulatory community
- Conduct pilots (EMA work program 2012)



## Conclusions?

- Not a panacea, not necessarily a route for *all* drugs, one size doesn't fit all,
- but might help regulators avoid the reputation trap (“too fast and too slow”),
- if properly managed and *communicated*, might be the best (or only?) option to balance the regulators’ *gatekeeper* and *enabler* roles.

**Thank you!**

