Policy Based "Pull" Incentives for Creating Breakthrough CNS Drugs

Jan 20, 2015
Financial Incentives Workshop
Neuroscience Forum, IOM
Washington, DC

Dennis W. Choi, MD, PhD
SUNY Stony Brook

Stony Brook
Neurosciences Institute

Key Assumptions

- There is an ongoing withdrawal of pharmaceutical companies from CNS drug R&D. This is a big problem.
  - 6/10 largest companies with 4/5 largest CNS drug pipelines (2009)
  - Reduced ability to develop needed treatments for CNS diseases
  - Biotech companies are thriving, but cannot compensate for loss of:
    - Total R&D resources (=NIH), impact across the academia-industry "ecosystem"
    - Late state chemistry and large-scale clinical trial capabilities
- While CNS drug development is difficult, it is feasible
  - Many approaches in R&D pipelines, appropriate for clinical testing
  - Decisions to withdraw based on sector risk/reward calculus – some large companies staying the course
- Enhancing "pull incentives" for breakthrough, high-medical impact drugs would help reduce or reverse Pharma withdrawal from the CNS sector
- Enhanced pull incentives can be crafted such that costs and medical risks are acceptable to patients. Both will be ameliorated by the benefits of successful drugs (HIV drugs; 5y delay in AD onset worth $447B by 2050)

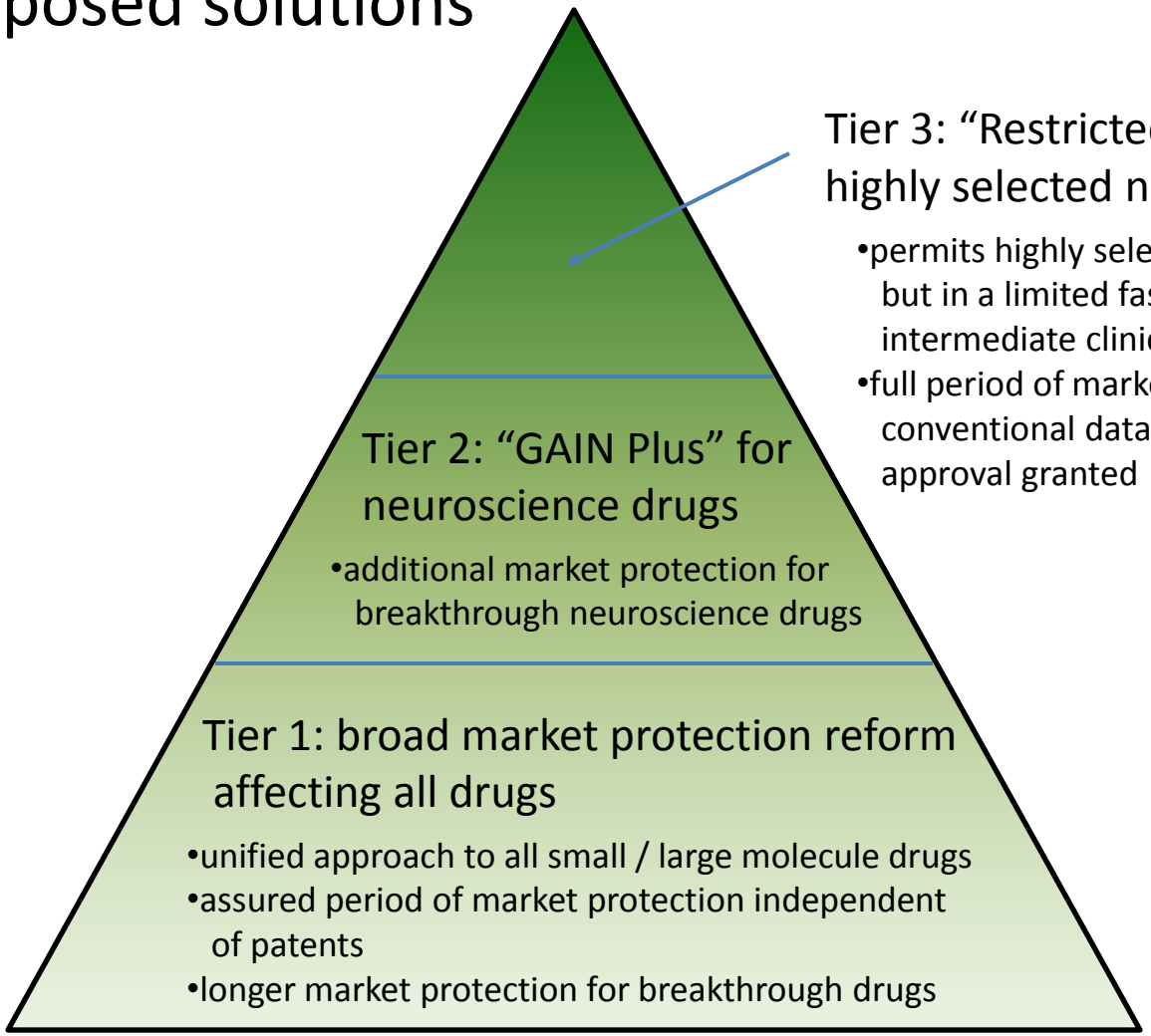
Risk/reward calculus: On the cusp

- In the 1990s, neuroscience was a cornerstone sector for most Pharma companies, driven by large market potential and major successes
  - Between 1995-2002, Pharma R&D doubled from $2.5B to $5.3B
  - Regulatory success rate for CNS drugs entering the clinic between 1993-2004 was 8.2% (CV 8.7%, GI/metabolic 9.4%, respiratory 9.9%)
- But recent failures, coupled with relatively high costs and shorter periods of market protection (lengthy trials and regulatory review - 24.5m vs 17.7m for CV and 8.1m for oncology) has led to a shift in R&D investment away from CNS

Focus: "*art of the doable*"

- $ -- not how to improve R&D, underlying science
- Pull incentives -- not push
  - Push incentives lower risks by directly supporting R&D (grants, tax breaks, investments in related research or infrastructure)
  - Pull incentives increase market returns
- Stroke of a pen (policy-based), not requiring upfront public funding
  - Advance market commitments and prize mechanisms out of present scope
  - Paper briefly discussed avenues for enhancing push incentives (committing to existing tax credits, increasing private investment through SRI vehicles) that would likewise not require public funding
- US market and policies

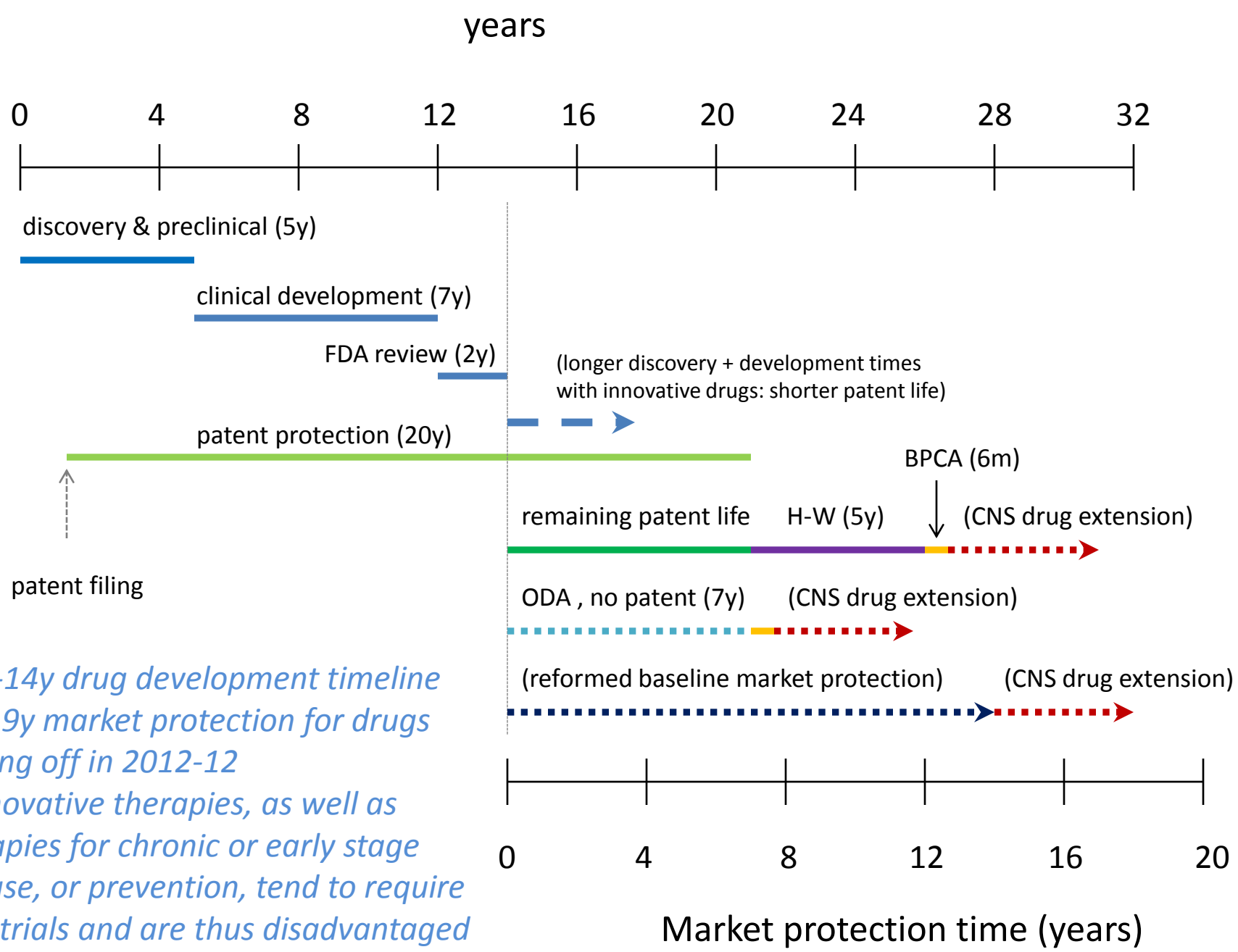
Proposed solutions



Tier 3: "Restricted Accelerated Approval" for highly selected neuroscience drugs

- permits highly selected drugs to be marketed early but in a limited fashion on the basis of biomarker or intermediate clinical data
- full period of market protection available when conventional data attained and regular approval granted

Precedents: "Biosimilars Act" (Biologics Price Competition and Innovation) of 2010 provides new biological therapies with 12y market protection beginning with FDA approval.
EMA "8+2+1" market protection.



- *11-14y drug development timeline*
- *12.9y market protection for drugs coming off in 2012-12*
- *Innovative therapies, as well as therapies for chronic or early stage disease, or prevention, tend to require long trials and are thus disadvantaged*

Sector specific market protection boosts: “GAIN Plus”

- Restricted to breakthrough, high medical impact CNS drugs
- Precedents: Orphan Drug Act 1983, pediatric exclusivity 2002 (Best Pharmaceuticals for Children Act), GAIN Act 2012(Generating Antibiotic Incentives Now).
  - 5y NCE data package protection: independent of patents but effective duration typically <= Hatch-Waxman
- Bugs & Brains now – something else later.
  - Should not be framed as sector-competitive
  - Current need to facilitate CNS and antibiotic drug development illustrates the desirability of developing a flexible market protection system that can be adapted dynamically to society’s changing medical needs

Restricted Accelerated Approval

- Modified, highly selective harnessing of AA pathway, created in 1992 to speed access to HIV drugs
  - Qualifying drugs (unmet, serious medical needs) approved based on surrogate biomarker endpoints, with confirmatory studies post marketing
  - 1996 FDA empowered to apply AA aggressively to oncology drugs (35 by 2010)
  - Recent FDA initiative to utilize cognitive battery in early AD as the basis for AA
- Approval stringently restricted beyond AA precedents, limiting pricing and use while additional clinical data collected, but permitting some recovery, ideally covered by payors, prior to full approval
  - full approval conveys a full period of market protection
  - ? progressive removal of restrictions – “adaptive approval” (PCAST, 2012)
  - ? acceptability to patients (medical risk), payors

Workshop Goals

- Examine (but do not work) background assumptions
  - Take stock of issues for pursuit in subsequent venues
- Begin to work candidate pull incentives
  - Are the solution proposed headed in the right direction?
- **Call to Action**: get to concrete next steps (as consensus permits)
  - What actions can individuals and organizations take now to advance momentum for policy changes?
    - Patient groups and foundations, supported by academic societies and industry advisors. Broad engagement of disciplines and stakeholders.
    - The slope ahead is steep. The public is recurrently reminded of examples of industry excesses. Emphasizing that the changes are to benefit patients, not industry will help. Industry concessions would also help.
  - What discussions can the IOM (through the neuroscience and drug fora) facilitate in the months ahead?