

2020 SOA Virtual Health Meeting

KERRI MILLER, PHARMD, BLUEPRINT MEDICINES CORP.

IAN SMITH, FSA, MAAA, OPTUM ADVISORY SERVICES

GREGORY WARREN, FSA, MAAA, OPTUM ADVISORY SERVICES

**Traditional Drug Development Process:
An Overview for Actuaries by Actuaries**

June 9, 2020



SOCIETY OF ACTUARIES

Antitrust Compliance Guidelines

Active participation in the Society of Actuaries is an important aspect of membership. While the positive contributions of professional societies and associations are well-recognized and encouraged, association activities are vulnerable to close antitrust scrutiny. By their very nature, associations bring together industry competitors and other market participants.

The United States antitrust laws aim to protect consumers by preserving the free economy and prohibiting anti-competitive business practices; they promote competition. There are both state and federal antitrust laws, although state antitrust laws closely follow federal law. The Sherman Act, is the primary U.S. antitrust law pertaining to association activities. The Sherman Act prohibits every contract, combination or conspiracy that places an unreasonable restraint on trade. There are, however, some activities that are illegal under all circumstances, such as price fixing, market allocation and collusive bidding.

There is no safe harbor under the antitrust law for professional association activities. Therefore, association meeting participants should refrain from discussing any activity that could potentially be construed as having an anti-competitive effect. Discussions relating to product or service pricing, market allocations, membership restrictions, product standardization or other conditions on trade could arguably be perceived as a restraint on trade and may expose the SOA and its members to antitrust enforcement procedures.

While participating in all SOA in person meetings, webinars, teleconferences or side discussions, you should avoid discussing competitively sensitive information with competitors and follow these guidelines:

- **Do not** discuss prices for services or products or anything else that might affect prices
- **Do not** discuss what you or other entities plan to do in a particular geographic or product markets or with particular customers.
- **Do not** speak on behalf of the SOA or any of its committees unless specifically authorized to do so.
- **Do** leave a meeting where any anticompetitive pricing or market allocation discussion occurs.
- **Do** alert SOA staff and/or legal counsel to any concerning discussions
- **Do** consult with legal counsel before raising any matter or making a statement that may involve competitively sensitive information.

Adherence to these guidelines involves not only avoidance of antitrust violations, but avoidance of behavior which might be so construed. These guidelines only provide an overview of prohibited activities. SOA legal counsel reviews meeting agenda and materials as deemed appropriate and any discussion that departs from the formal agenda should be scrutinized carefully. Antitrust compliance is everyone's responsibility; however, please seek legal counsel if you have any questions or concerns.

Presentation Disclaimer

Presentations are intended for educational purposes only and do not replace independent professional judgment. Statements of fact and opinions expressed are those of the participants individually and, unless expressly stated to the contrary, are not the opinion or position of the Society of Actuaries, its cosponsors or its committees. The Society of Actuaries does not endorse or approve, and assumes no responsibility for, the content, accuracy or completeness of the information presented. Attendees should note that the sessions are audio-recorded and may be published in various media, including print, audio and video formats without further notice.

Agenda

Introduction & Background

Research & Discovery

Development & Approval

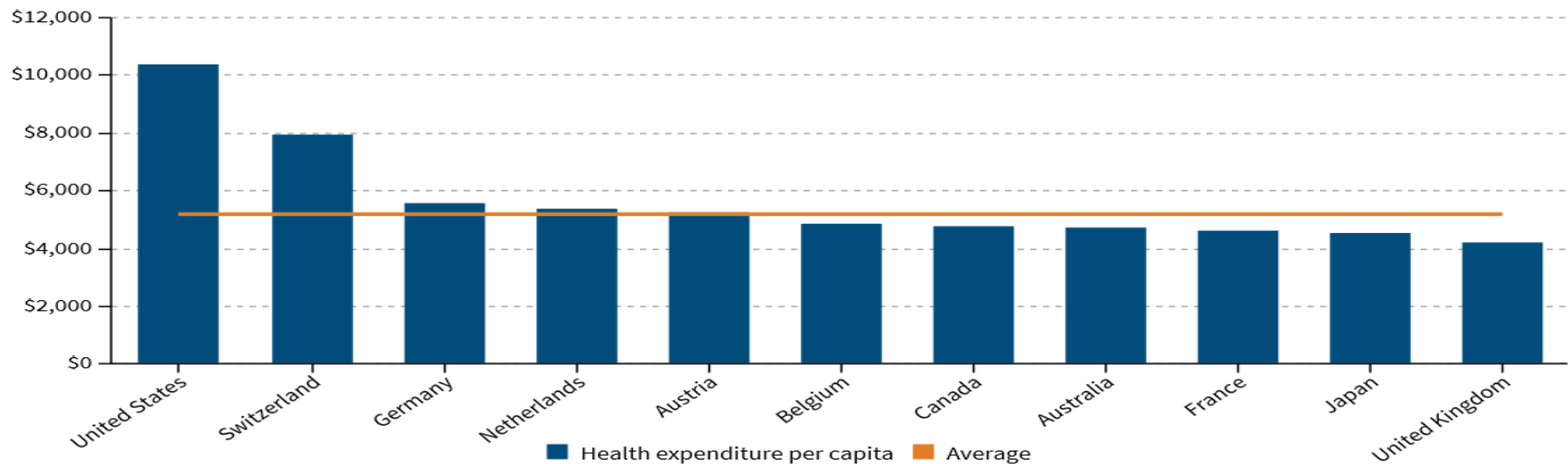
Drug Development Costs

Initiative 18/11: Actuarial Perspectives on Prescription Drug Financing

The United States spends roughly twice as much as comparable countries on a per capita basis—18 percent of gross domestic product (GDP) in the United States is spent on health care, compared to 11 percent of GDP in comparable countries.

Figure 1: Health Consumption Expenditures Per Capita, U.S. Dollars, PPP Adjusted, 2017

Hover Over Image for Specific Data



Source: Sawyer, Bradley, and Cynthia Cox, *How Does Health Spending in the U.S. Compare to Other Countries?* *Peterson-KFF Health System Tracker*, December 7, 2018 (accessed August 2, 2018).

The Society of Actuaries (SOA) joined forces with the Kaiser Family Foundation (KFF) in 2017 to charter Initiative 18|11: What Can We Do About the Cost of Health Care? The Healthcare Financing Management Association (HFMA) later joined the effort.

Initiative 18/11: Actuarial Perspectives on Prescription Drug Financing

The inaugural event for Initiative 18|11 occurred on March 7, 2018, in Washington, D.C.

- The meeting attendees included more than 30 thought leaders throughout the health care community, including actuaries, health economists, employee benefits experts and hospital administrators.
- Participants focused on two key drivers: the price of goods and services and the chronic disease burden.
- Participants also noted that fragmentation of care within the United States can result in unnecessary administrative expenses and make finding solutions more difficult.
- Several participants lamented the lack of transparency in the current health care system, especially in terms of how pharmacy prices are determined.
- With that in mind, the Initiative 18|11 leadership, along with the Health Section Council of the SOA, launched a strategic initiative entitled “**Actuarial Perspectives on Prescription Drug Financing**” to document and analyze the underlying process.

Actuarial Perspectives on Prescription Drug Financing: 4 Research Areas

- 1 Drug Development Process** — what are the phases of the drug development process, what happens in each, how does it all end up in a new therapy on the market and what does it cost?
- 2 Economic Impact** — how much is spent on prescription drugs in the United States, what are the various ways of measuring and reporting that, how is it changing over time and what is driving that change?
- 3 Consumer Impact** — what is “direct-to-consumer” pharmaceutical advertising, what are manufacturer coupons and patient assistance programs, what are point-of-sale rebates and how do they all affect consumers in the United States?
- 4 Regulatory Process** — what regulatory bodies exist at the state and federal level in the United States, what are their areas of oversight and what roles do they play in the pharmacy eco-system of the United States?

Actuarial Perspectives on Prescription Drug Financing: Series of Articles

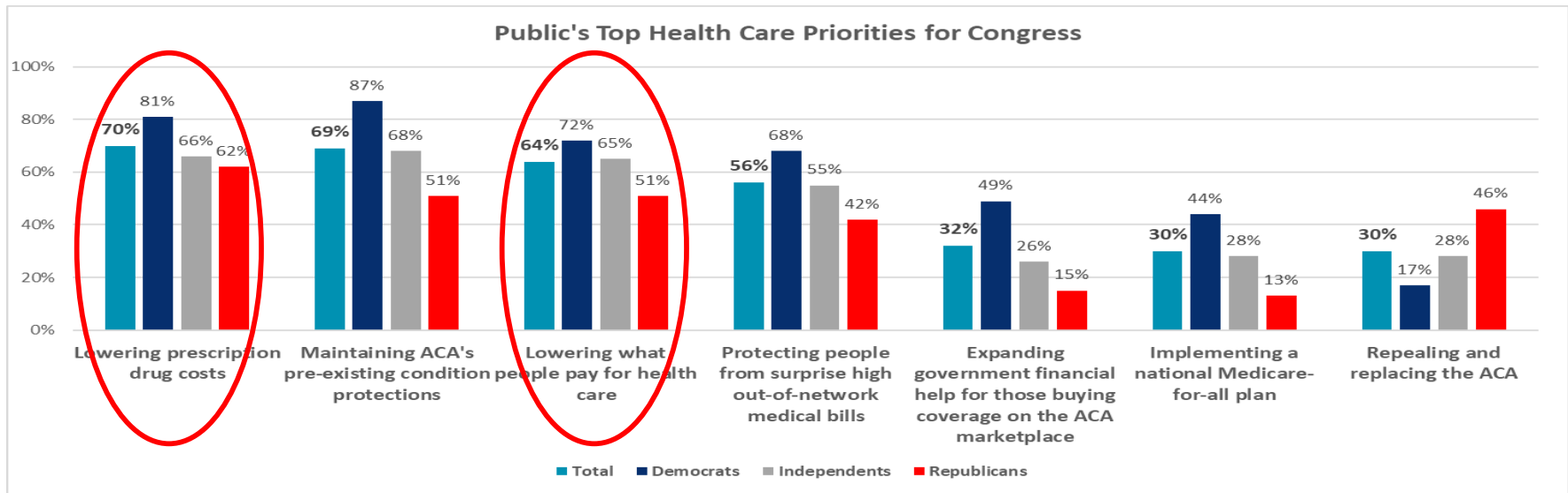
“The Actuary” Web Exclusive Series entitled “Actuarial Perspectives on Prescription Drug Financing” was published in May 2020 with the following articles:

1. Traditional Drug Development Process (Drug Development Process)
2. Too Much or Too Little? (Economic Impact)
3. What is the Price Anyway? (Economic Impact)
4. Trends in Prescription Drug Spending (Economic Impact)
5. Direct-to-Consumer Pharmaceutical Advertising (Consumer Impact)
6. Manufacturer Coupons and Patient Assistance Programs (Consumer Impact)
7. Rebates at the Point of Sale (Consumer Impact)

Additional research is underway with anticipated articles on the following topics to be published later in 2020:

1. Specialty and Precision Medicine Development Process (Drug Development Process)
2. State and Federal Regulatory Oversight Process (Regulatory Process)
3. Additional Global Comparisons?? Other Topics??

Actuarial Perspectives on Prescription Drug Financing: Lessons Learned



Source: [Kirzinger, Ashley, Audrey Kearney, and Mollyann Brodie. KFF Health Tracking Poll – September 2019: Health Care Policy in Congress and on the Campaign Trail. Kaiser Family Foundation, September 12, 2019 \(accessed April 8, 2020\).](#)

Four areas actuaries can uniquely and positively contribute:

Increasing transparency

Encouraging competition

Aligning stakeholder incentives

Mitigating total cost of care increases

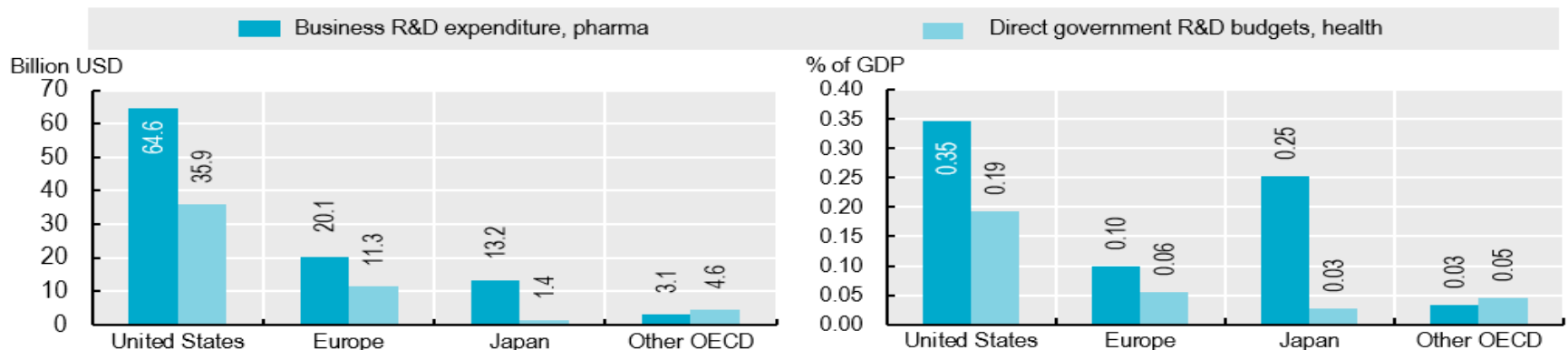
Traditional Drug Development Process: History of Medicines

1. Types of medicine:
 - Initially natural with mixed results
 - Now traditional medicines developed from nature with scientific approach
2. Ideas used to come from active ingredients of existing remedies or serendipitous discoveries
3. More recently drug discovery comes from more definitive laboratorial progression steps:
 - Identifying and validating a target
 - Generating assays to find lead compounds
 - Optimizing lead compounds to increase affinity and efficacy and reduce potential side effects
4. More complex discovery processes require more time and capital investment
5. Expanded skill sets now leveraged in drug discovery process:
 - chemists,
 - physiologists
 - statisticians
 - biochemists
 - Molecular biologists
 - toxicologists
 - pharmacologists
 - computer scientists leveraging data from chemical libraries and gene sequencing efforts

Traditional Drug Development Process: Funding Mechanisms

1. Historically, government and philanthropic organizations funded early basic discovery
2. Pharmaceutical companies and venture capitalists funded drug discovery and late-stage development.
3. Increased costs have led to increased venture capital involvement
4. Direct and/or indirect public funding (mainly through National Institutes of Health) still exists to some degree in at least the early stages for almost every drug that comes to market
5. In 2016 over \$150 Billion invested worldwide in drug research and development when public and private funding sources are combined

Figure 1: Business and Government R&D Spending



Health at a Glance 2019 ©OECD 2019. Chapter 10, Figure 10.12. Business enterprise expenditure for pharmaceutical R&D (BERD) and government outlays for health related R&D (GARD), 2016 (or nearest year). Version 1. Last updated: 03-Nov-2019.

Agenda

Introduction & Background

Research & Discovery

Development & Approval

Drug Development Costs

Audience Analysis - Polling Question

Q: How familiar are you with the drug development process?

1. Not familiar at all
2. Basic familiarity
3. Working knowledge
4. Extremely knowledgeable

Research & Discovery



Disease Target Identification & Validation



Protein (receptor) that performs a biological function



Drugs attack or modify the target protein that leads to disease



Target ideas

Academic research
Scientific literature
Bioinformatics data mining

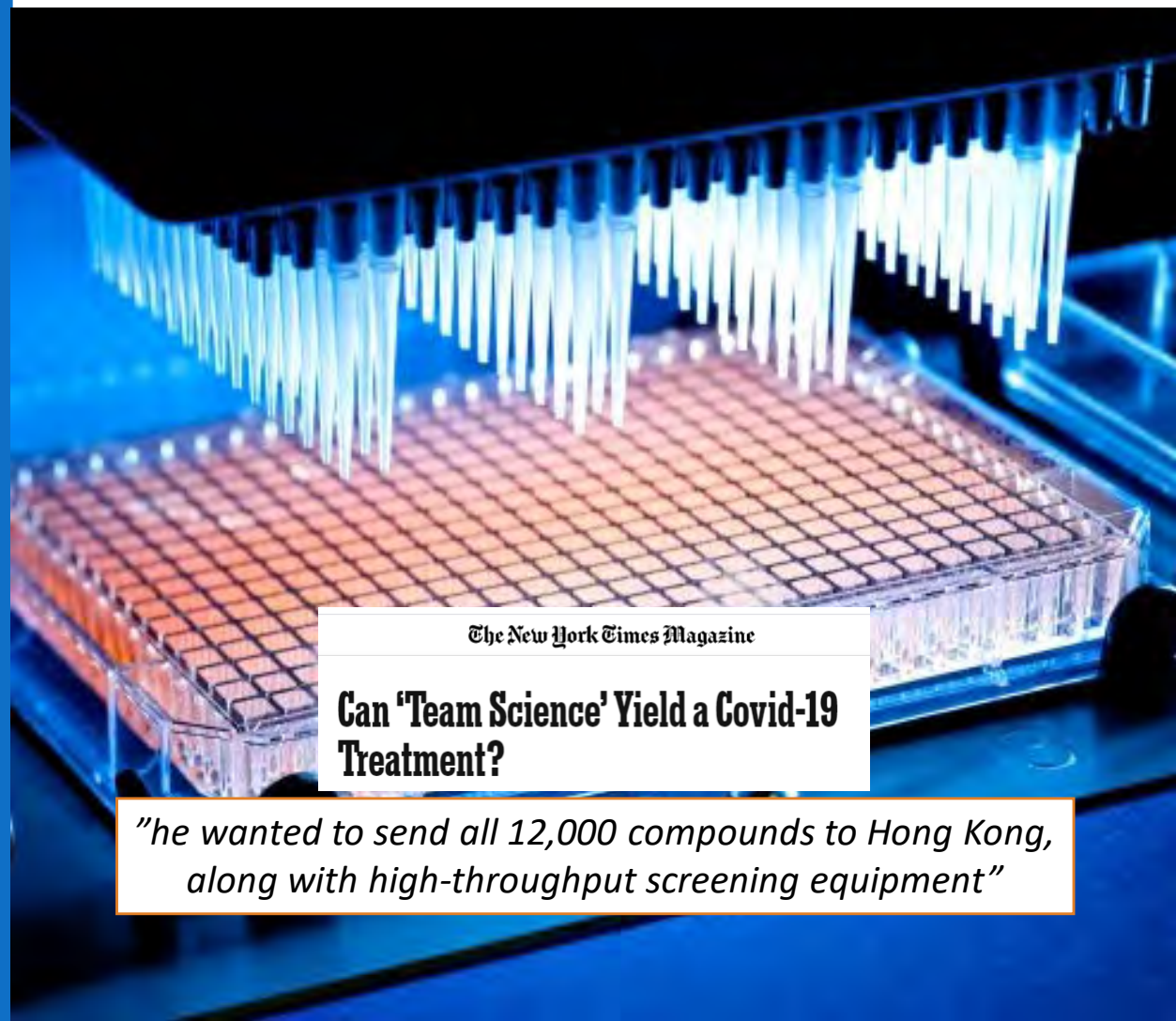


Artificial Intelligence

Lead Compound Screening

Two top screening methods are high-throughput screening (HTS) and knowledge-based screening.

HTS uses automated robotics to quickly perform millions of assays to match the drug-like properties with libraries of compounds.

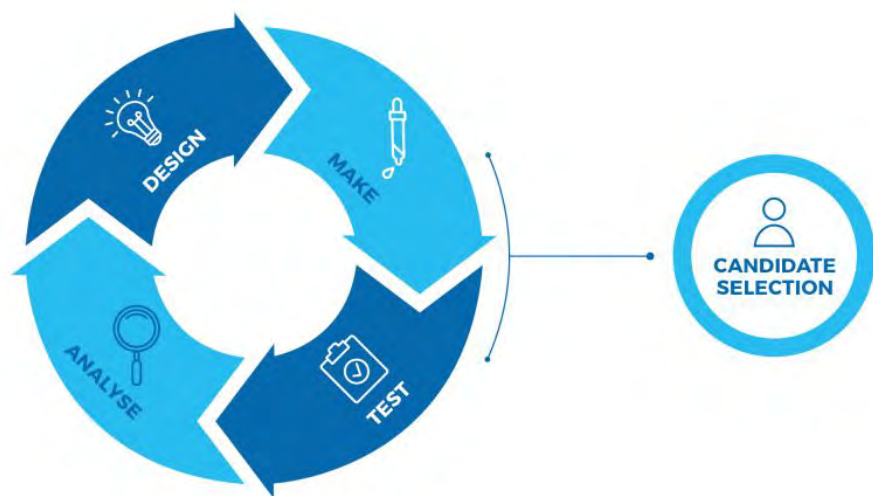


The New York Times Magazine

Can 'Team Science' Yield a Covid-19 Treatment?

"he wanted to send all 12,000 compounds to Hong Kong, along with high-throughput screening equipment"

Lead Compound Optimization

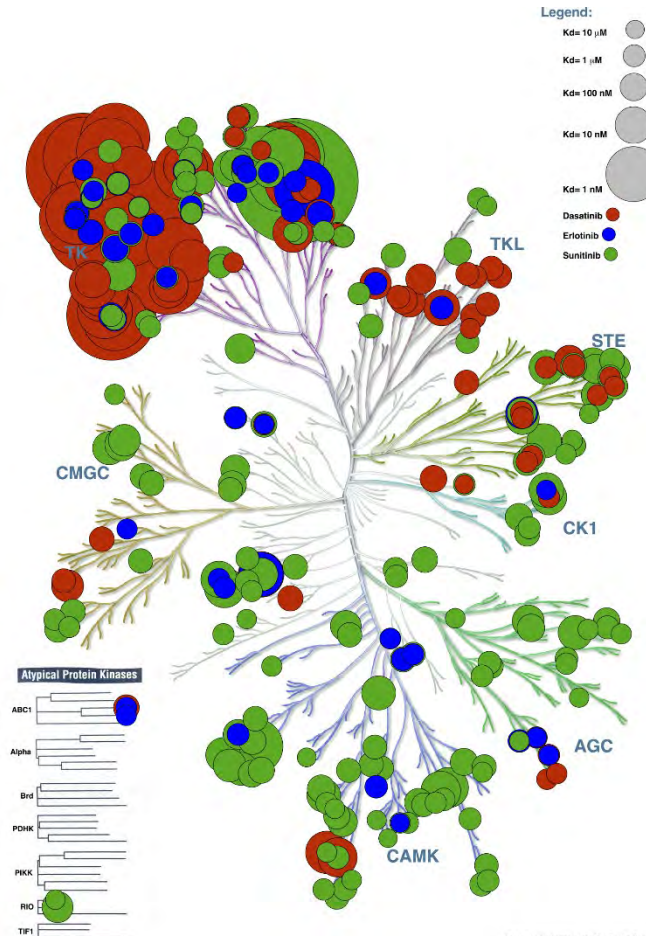


Iterative rounds of synthesis

- How potent/selective to the target protein vs. non-target proteins
- Select the one that most actively binds to the target

Example: Protein Kinase “family tree”

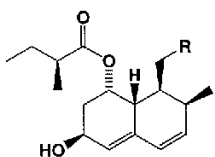
- Regulate multiple biological processes
- Cancer often involves alterations in kinase activity
- Kinases represent important targets in drug design



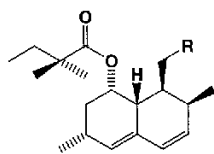
*Illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

<https://doi.org/10.7717/peerj.126/fig-6>

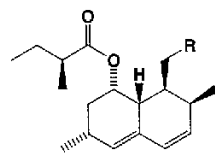
Lead Compound Optimization



Pravastatin (acid) (R=b)
Pravastatin lactone (R=a)



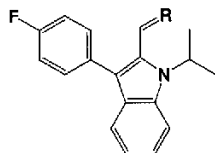
Simvastatin (lactone) (R=a)
Simvastatin acid (R=b)



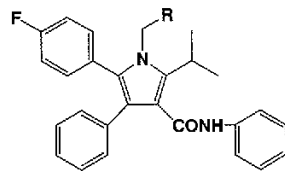
Lovastatin (lactone) (R=a)
Lovastatin acid (R=b)

Structure modifications

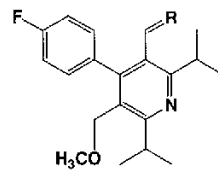
- properties to balance out intensity, specificity, toxicity, instability, etc.



Fluvastatin (acid) (R=b)
Fluvastatin lactone (R=a)



Atorvastatin (acid) (R=c)
Atorvastatin lactone (R=a)



Cerivastatin (acid) (R=b)
Cerivastatin lactone (R=a)

Agenda

Introduction & Background

Research & Discovery

Development & Approval

Drug Development Costs

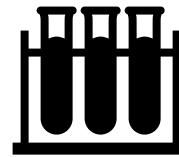
Development and Approval



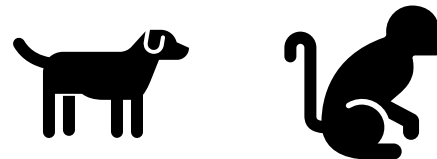
Pre-Clinical Studies

- Preliminary efficacy, toxicity, pharmacokinetic and pharmacodynamic information
- Failure reasons: excessive toxicity

- In vitro testing



- In vivo testing



Investigational New Drug (IND) Request

Start of human clinical trials

All pre-clinical study info and data

Needed to ship experimental drug across state lines

20-year patent exclusivity begins upon IND approval.

Clinical Trials



Phase 1

Few dozen healthy volunteers – PK/PD

Max effective dose



Phase 2

100s of patients with disease of interest

Establish optimal dose



Phase 3

100s to 1000s of pts with disease

FDA defines endpoints to determine success/failure

Drug Denials - Polling Question

Q: Which is NOT a reason a drug might be denied approval by the FDA?

1. Too expensive
2. Safety concerns
3. Manufacturing issues
4. Lack of efficacy

New Drug Application (NDA)

Expedited review opportunities via 1992 Prescription Drug User Fee Act (PDUFA)

- Fast Track designation
- Accelerated Approval
- Priority Review
- Breakthrough Therapy designation

File after phase 2 or phase 3 results are promising.



Key Factors FDA considers:

Data gathered during animal studies	Phase 1/2/3 study results	Drug abuse potential	Manuf. info	Proposed label indication and use
-------------------------------------	---------------------------	----------------------	-------------	-----------------------------------

FDA Post-Market Safety Monitoring



Routine inspections of
manufacturing facilities



Monitors

Drug advertisements
Promotional activity
Safety reports



Actions

Warning letters
Product seizure
Criminal prosecution/fines

Key Goals:

Ensure continued effectiveness.

Inform consumers about side effects or
problems.

Agenda

Introduction & Background

Research & Discovery

Development & Approval

Drug Development Costs

Topics for discussion

Topics
Drug Development Costs and relationship to price
Drug Types and relationship to price
Other pricing considerations
Actuarial consideration of prices

Drug Development Costs and Relationship to Price

1. Costs of developing a new pharmaceutical vary drastically
 - a) One study of cancer prescriptions estimated \$1.4B per approved drug (DiMasi, et al 2013)
 - b) Another estimated \$760M (Prasad, et al 2017)
2. Other studies have focused on the treatment of more broad categories and have found that rare disease treatments can have \$170M and non-orphan costs are around \$290M
 - a) The discrepancy seems to be largely around the cost of research and development and differing approval processes
3. In many industries the cost of development, materials, and labor would be enough to ascertain what these drugs should cost. However, in the United States there are other considerations...

Drug Development Costs and Relationship to Price

1. In the United States the free market is allowed to determine the cost of goods
2. As such the price of drugs is largely determined by what the market will bare for a particular drug and has relatively little to do with the costs of bringing the particular drug to market
3. What is used to determine what the market will bare is based on many factors
 - a) Type of drug being developed and its relationship to others already on the market
 - b) Type of drug being developed and its relationship of the new drug to others in its therapeutic class
 - c) Other drug pricing considerations

Drug Type: New Drug to Saturated Market

Scenario

- Population is known
- Direct drug competitors already on the market

Example

- Additional SGLT-2s to diabetes market

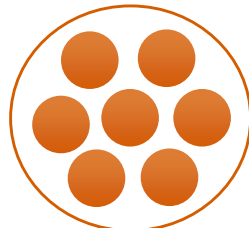
Actuarial Methods

- Use historical experience to anticipate cost and frequency

Pharmacy Could Provide...

- No big/changing events, so no need for external info

Current Utilizing



Population



New Drug



Drug Type: New Method of Action (MOA) to Established Market

Scenario

- Population is known
- *No direct drug competitors* on the market

Example

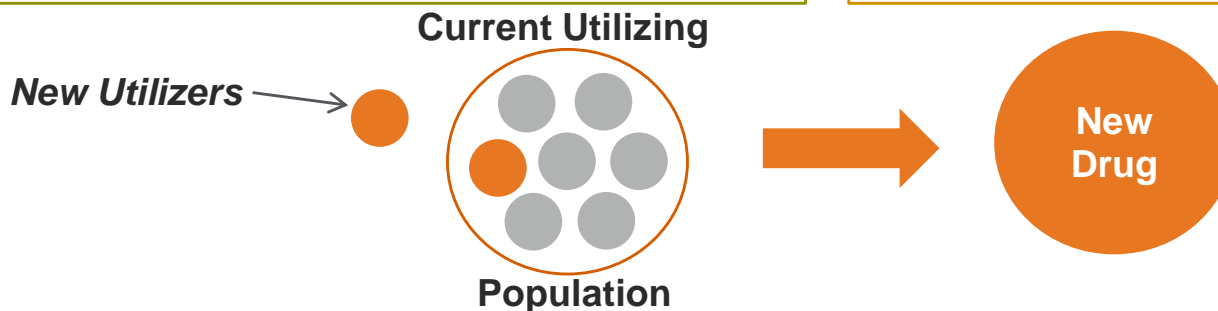
- New oral product in RA

Actuarial Methods

- Estimate shift to new drug using similar scenarios for different drugs
- Estimate cost using published reports, expert opinion (i.e. Health Technology Pipeline)

Pharmacy Could Provide...

- Expected shift percent
- Expected costs



Drug Type: New MOA to Unsatisfied Market

Scenario

- Population is *unknown*
- *No direct drug competitors* on the market

Example

- First Launches of New Hepatitis C

Actuarial Methods

- Similar to New MOA in established market
- Additionally, estimate “warehoused” population through historical diagnoses and online research

Pharmacy Could Provide...

- Expected shift percent & costs
- Estimate of disease in total insured population



Other Pricing Considerations

Institute for Clinical and Economic Review (ICER) is a Boston-based institute that describes itself as “a trustworthy, independent source to help assess how valuable a new drug really is.”

ICER evaluates the clinical and economic value of prescription drugs, medical tests, and other health care and health care delivery innovations.

ICER produces drug assessment reports that provide an analysis of how well a drug works

- How much better is it than what we already have?
- How much could it save us?
- How much would it cost to treat everyone who needs it?

Reports give a price benchmark based on models used to determine long-term value-based approach to drug pricing

Actuarial Pricing Considerations

1. Actuaries can generally make fairly good predictions on the prices of new drugs within the market when taking into consideration a new drug's type, relationship to the existing market and relationship to other treatments in its therapeutic class
2. However, consistently updating assumptions and looking back on methodology to compare to actuals is needed
 - a) For example, new Hepatitis C therapies in 2013

Thank you.

Thank you.

Thank you.

Thank you.

Kerri Miller, PharmD
National Account Executive
Blueprint Medicines Corp.
720-427-0800
kkmiller000@gmail.com

Ian Smith, FSA, MAAA
Actuarial Manager
Optum Advisory Services
763-797-2478
ian.smith@optum.com

Gregory Warren, FSA, MAAA
SVP & Chief Actuary
Optum Advisory Services
303-256-0805
gregory.warren@optum.com





**SOCIETY OF
ACTUARIES®**