PORTAL
Program on Regulation, Therapeutics, and Law

DEPARTMENT OF MEDICINE
BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL

Market- & drug development-trends potentially affecting prices

Jonathan J. Darrow, SJD, LLM, JD, MBA

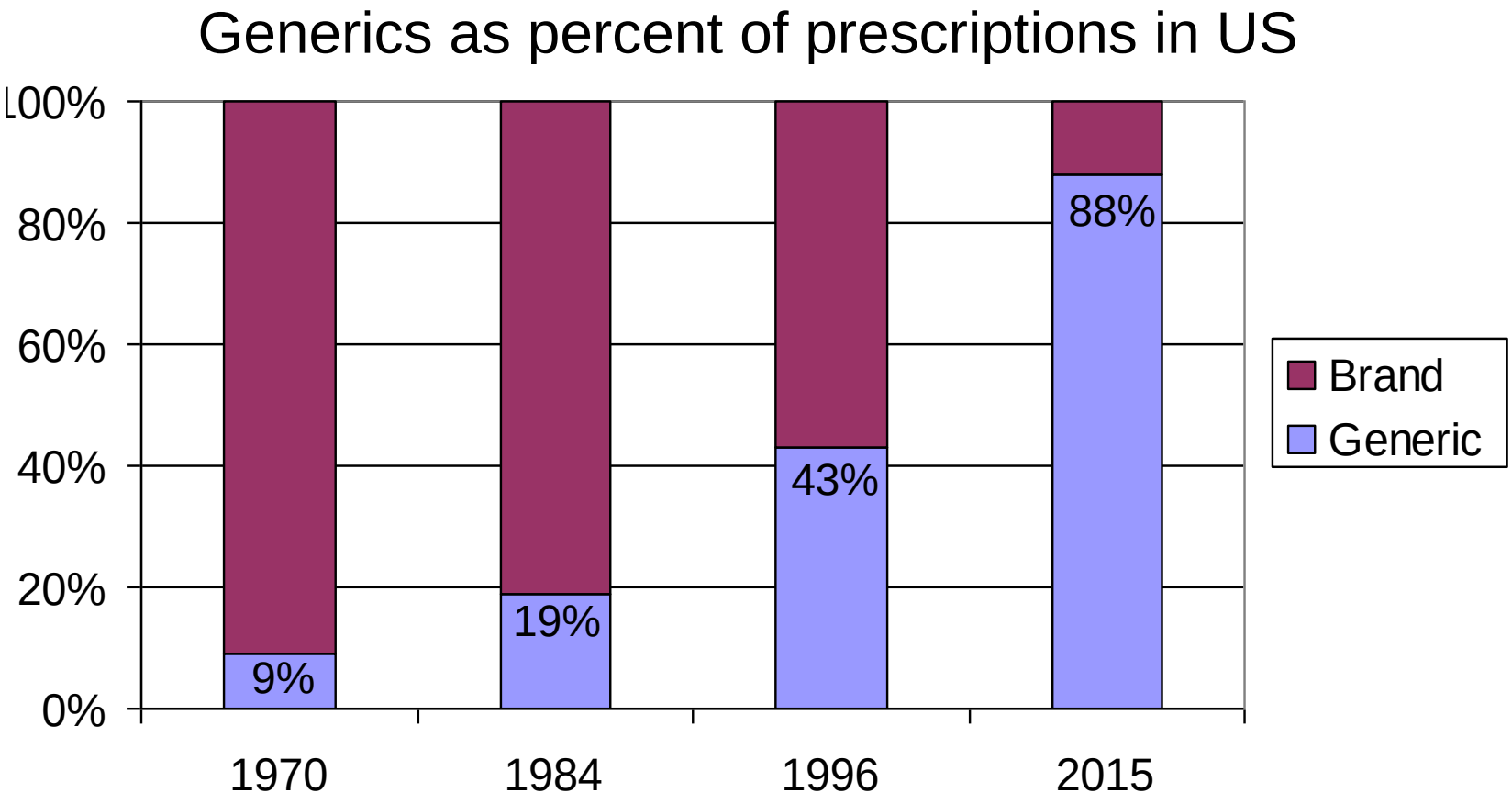
Faculty, Harvard Medical School
Program on Regulation, Therapeutics, & Law (PORTAL)
Brigham & Women's Hospital

DIVISION OF
PHARMACOEPIDEMIOLOGY &
PHARMACOECONOMICS

June 13, 2018

1. **Market trends affecting price**
2. Drug development trends

Market trend #1: Growing generic share

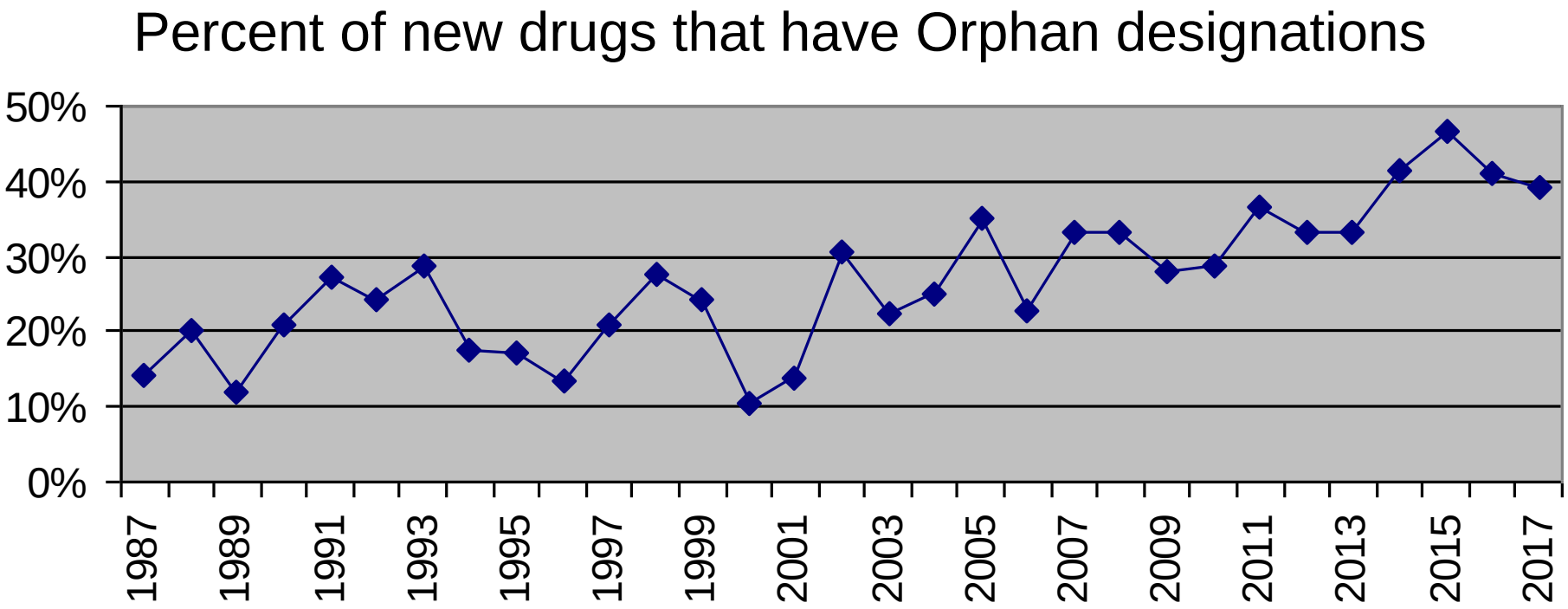


Brand-manufacturer profits come from a shrinking share of prescriptions.

Kesselheim AS, Darrow JJ. Hatch-Waxman turns 30: do we need a redesigned approach for the modern era? *Yale JHLPE 2015*:15(2):293-348 (see n.29) (1970, 1984, 1996 data)

Generic Pharmaceutical Association 2015 Annual Report, Feb. 2016, p.14 (2015 data)

Market trend #2: More orphan drugs



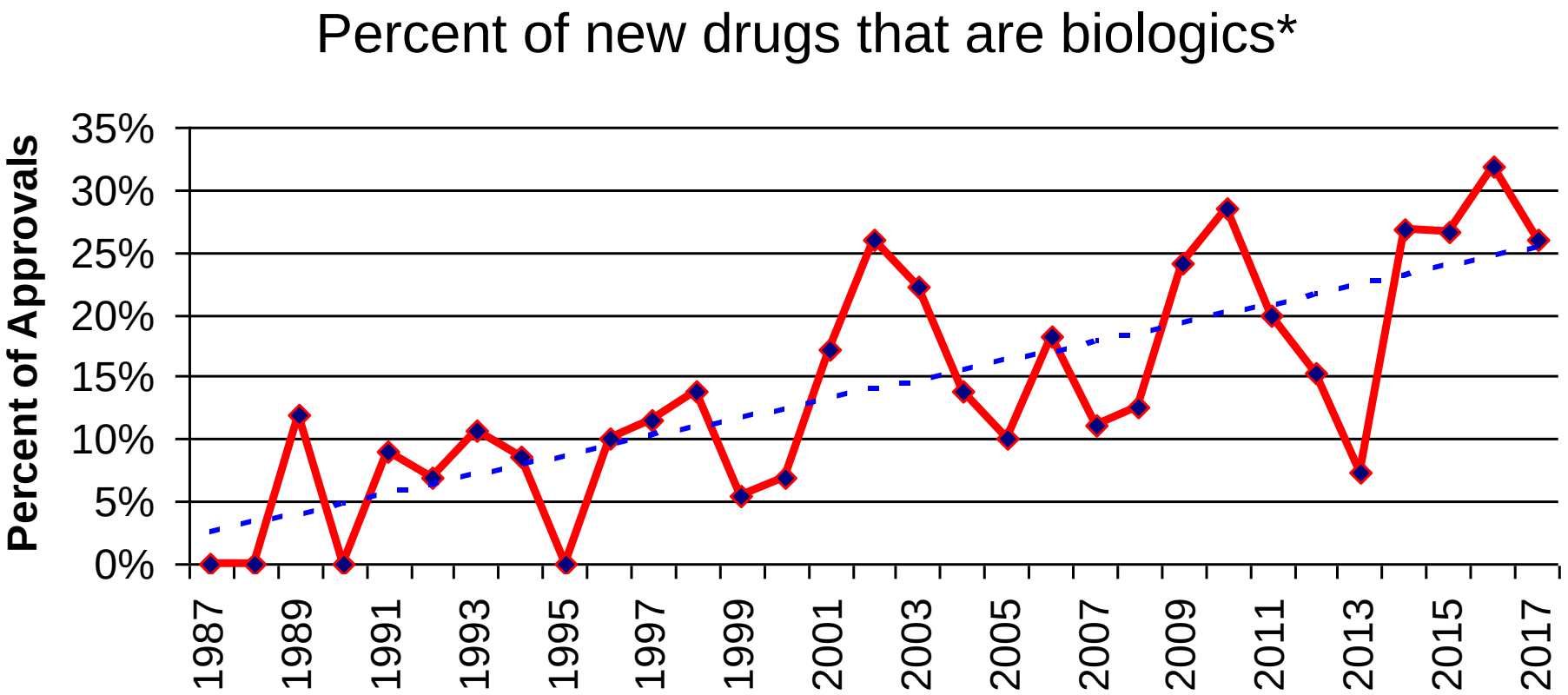
On average, profits come from a shrinking number of patients.

Revenues = Quantity x Price

Caveats (examples)

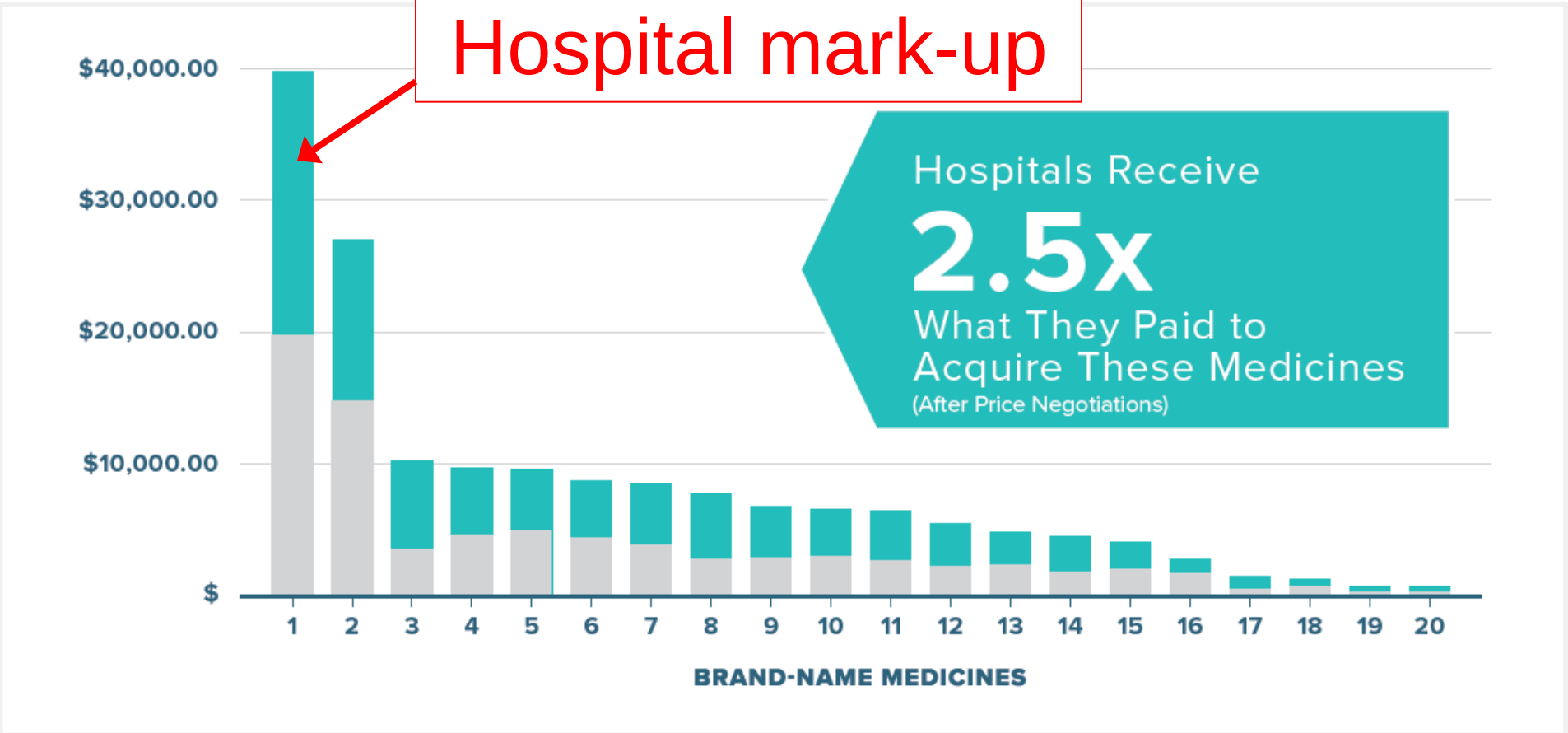
- Shrinking share, but total number of prescriptions has increased
- Some drugs have multiple orphan (or non-orphan) designations
  - E.g., Humira, Enbrel, Remicade, Crestor…

Market Trend #3: More biologics



Biologics can be more expensive to manufacture and administer.

*excludes biologics approved under an NDA, and vaccines or other CBER products



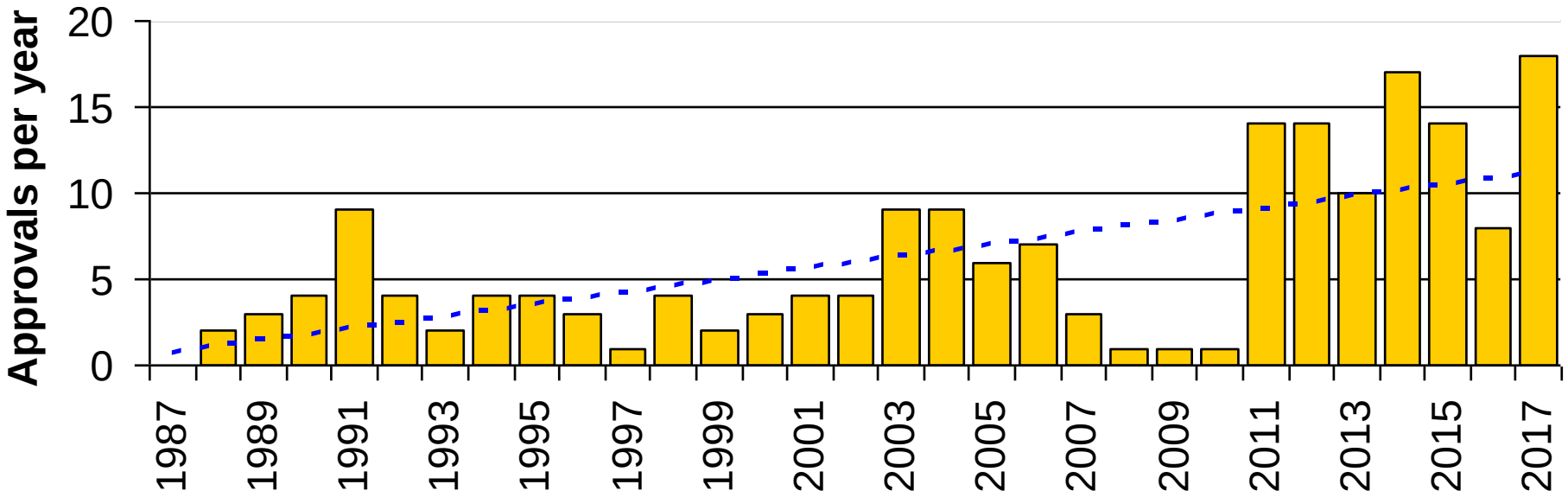
Moran Company, "Hospital Charges and Reimbursement for Drugs: Analysis of Mark Ups Relative to Acquisition Cost." October 2017.

From: https://www.phrma.org/graphic/hospitals-mark-up-medicine-prices-nearly-500

1. Market trends affecting price
2. **Drug development trends**

Drug development trend #2: More fast-track (1988) approvals*

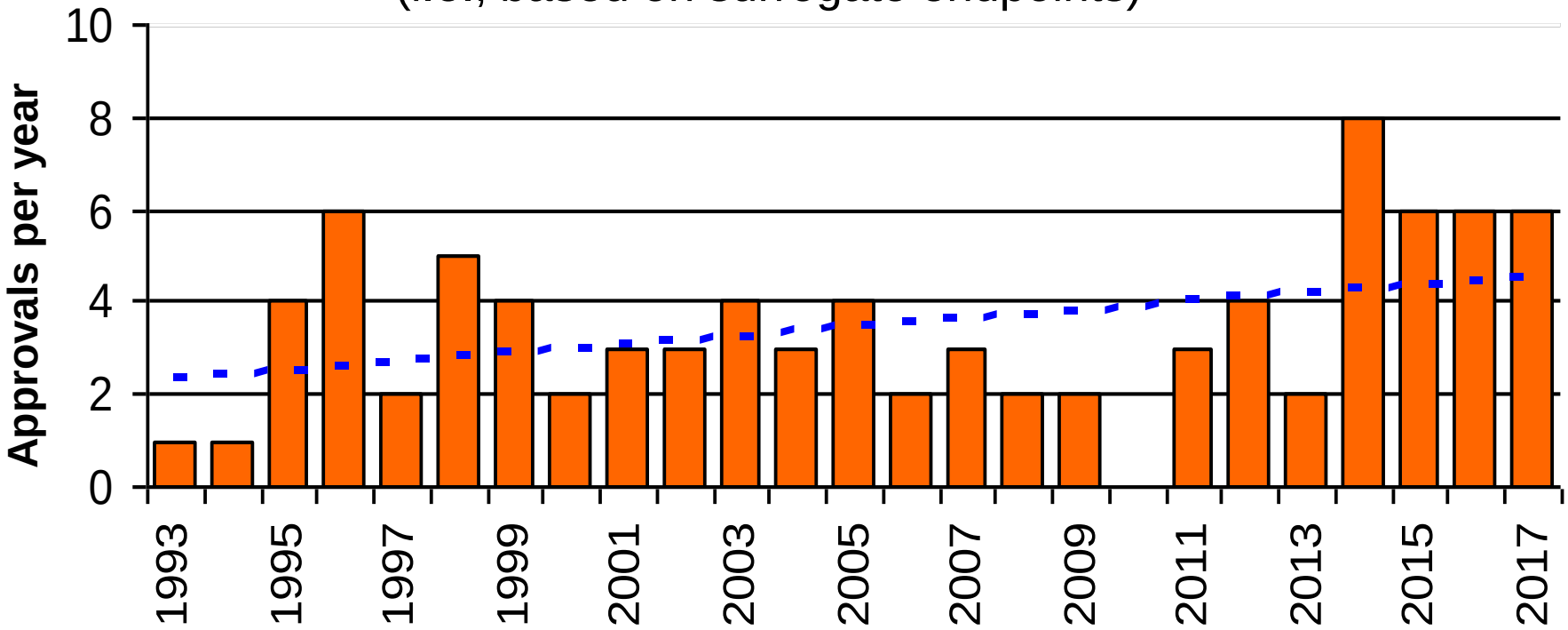
(can be based on Phase II trial)



*Darrow JJ, Kesselheim AS. Drug development and FDA approval, 1938–2013. *N Engl J Med* 2014;370(26):2465.

Drug development trend #1: More accelerated (1992) approvals*

(i.e., based on surrogate endpoints)



*Darrow JJ, Kesselheim AS. Drug development and FDA approval, 1938–2013. *N Engl J Med* 2014;370(26):2465.

Original Investigation | HEALTH CARE REFORM

JAMA Intern Med. 2015;175(8):1389-1398. doi:10.1001/jamainternmed.2015.2829

The Strength of Association Between Surrogate End Points and Survival in Oncology

A Systematic Review of Trial-Level Meta-analyses

Vinay Prasad, MD, MPH; Chul Kim, MD, MPH; Mauricio Burotto, MD; Andrae Vandross, MD

Surrogate Outcomes in Clinical Trials

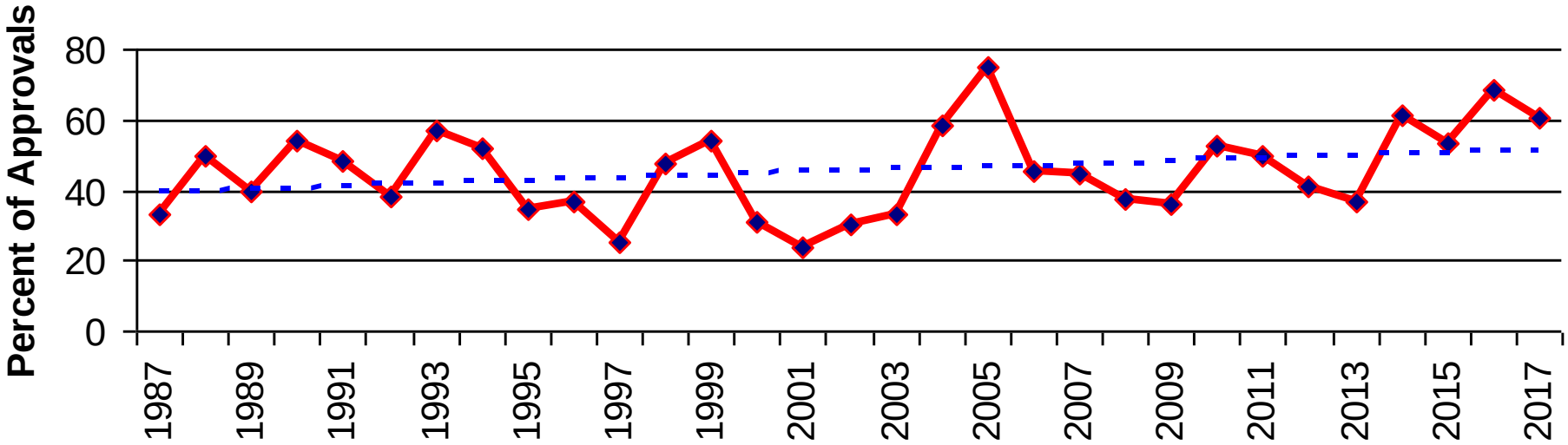
A Cautionary Tale

Staffan Svensson, MD, PhD
David B. Menkes, MD, PhD
Joel Lexchin, MSc, MD

JAMA INTERN MED/VOL 173 (NO. 8), APR 22, 2013

Drug development trend #3: More priority (1992) reviews*

(6 month FDA review, rather than 10 months)**



*Darrow JJ, Kesselheim AS. Drug development and FDA approval, 1938–2013. *N Engl J Med* 2014;370(26):2465.

** Prior to 1992, we considered “A” and “B” to be “priority” and “C” to be “standard”

Available online at www.sciencedirect.com
ScienceDirect
Journal of Health Economics 27 (2008) 175–200
JOURNAL OF HEALTH ECONOMICS
www.elsevier.com/locate/econbase

The risk we bear: The effects of review speed and industry user fees on new drug safety☆

Mary K. Olson*

Department of Economics, Tulane University, 306 Tilton Hall, 6823 St. Charles Avenue, New Orleans, LA 70118-5698, United States

Received 13 February 2006; received in revised form 12 October 2007; accepted 18 October 2007
Available online 22 January 2008

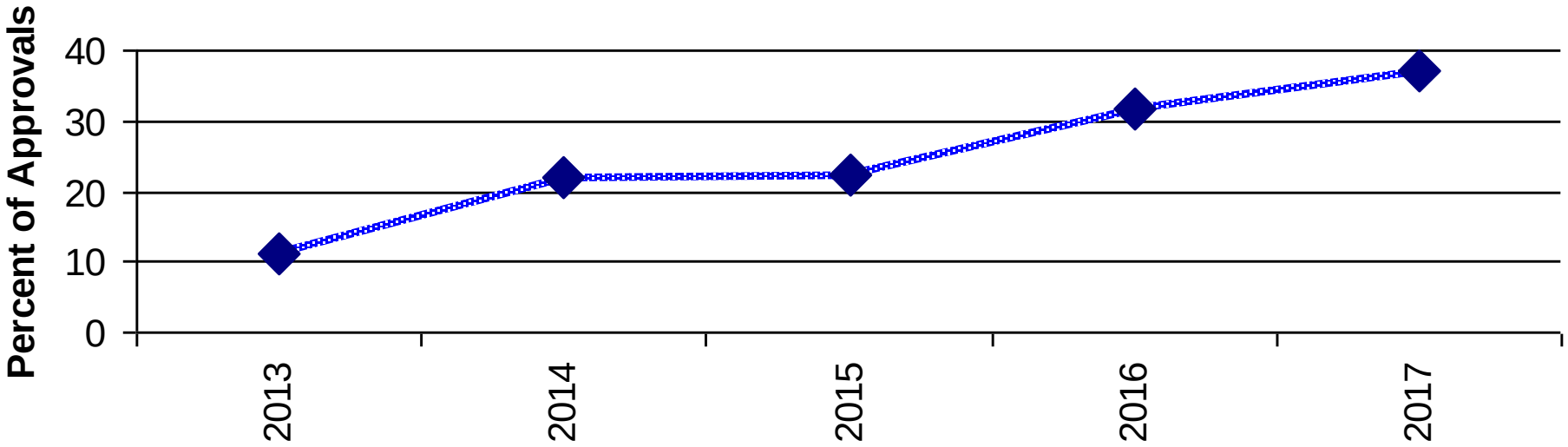
The Complications of Controlling Agency Time Discretion: FDA Review Deadlines and Postmarket Drug Safety

American Journal of Political Science, Vol. 56, No. 1, January 2012, Pp. 98–114

Daniel Carpenter Harvard University
Jacqueline Chattopadhyay Harvard University
Susan Moffitt Brown University
Clayton Nall Stanford University

Drug development trend #4: More “Breakthrough Therapies”*

(approval in 4.8 rather than 8.0 years**)



*Darrow JJ, Avorn J, Kesselheim AS. The FDA breakthrough drug designation: four years of experience. *N Engl J Med* 2018; 378(15):1444-1453.

**Hwang T, Darrow JJ, Kesselheim AS. The FDA’s expedited programs and clinical development times for novel therapeutics, 2012–2016. *JAMA* 2017;318(21):2137–8.

PRECISION MEDICINE

By Lisette Pregelj, Thomas J. Hwang, Damian C. Hine, Evan B. Siegel, Ross T. Barnard, Jonathan J. Darrow, and Aaron S. Kesselheim

DOI: 10.1377/hlthaff.2017.1580
HEALTH AFFAIRS 37,
NO. 5 (2018): 724–731

Precision Medicines Have Faster Approvals Based On Fewer And Smaller Trials Than Other Medicines

The NEW ENGLAND JOURNAL of MEDICINE

The FDA Breakthrough-Drug Designation — Four Years of Experience

Jonathan J. Darrow, S.J.D., J.D., M.B.A., Jerry Avorn, M.D.,
and Aaron S. Kesselheim, M.D., J.D., M.P.H.

- 52% based on Phase 1 or 2 (75%*)
- 45% based on single trial (75%*)
- 42% did not have either a placebo or active control (63%*)

*Oncology BT drugs

Implications for future spending

- Less data at time of approval
- Shift of data collection from Phase 3 to 4
- Less time for FDA to review each drug
- Result:
  - Greater uncertainty about risk/benefit
  - Payors must make decisions amid uncertainty

Increased pressure for payor coverage

- Uncertain benefit…
  - …but superlative labels
- "Breakthrough" designation can increase pressure for payor coverage*
  - E.g., pimavanserin (Nuplazid) (~$2800 / 30 days**)
  - E.g., ivacaftor/lumacaftor (Orkambi) (~$21,000 / 112 tablets)
  - E.g., uridine triacetate (Xuriden) (~$45,000 / 30 packets)
  - E.g., pirfenidone (Esbriet) ($27,000 / 270 tablets)

*Darrow JJ, Avorn J, Kesselheim AS. The FDA breakthrough drug designation: four years of experience. *N Engl J Med* 2018; 378(15):1444-1453.

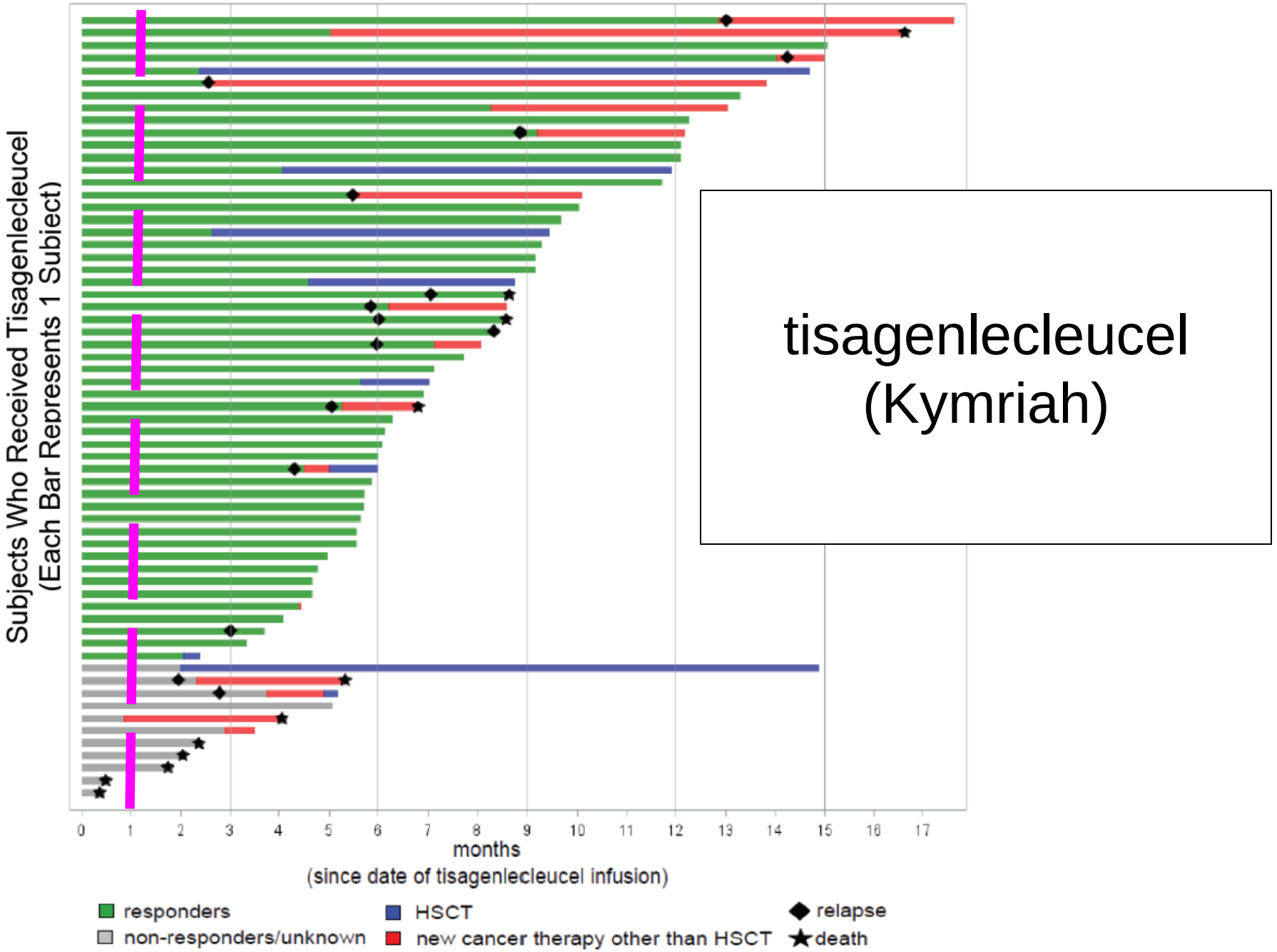
*Krishnamurti T, Woloshin S, Schwartz LM, Fischhoff B. A randomized trial testing US Food and Drug Administration "breakthrough" language. *JAMA Intern Med* 2015; 175: 1856-8.

** Prices from https://www.goodrx.com/

Required Medicare coverage*

1. Anti-convulsants
2. Anti-depressants
3. Anti-neoplastics [cancer medicines]
4. Anti-psychotics
5. Anti-retrovirals
6. Immunosuppressants for the treatment of transplant rejection

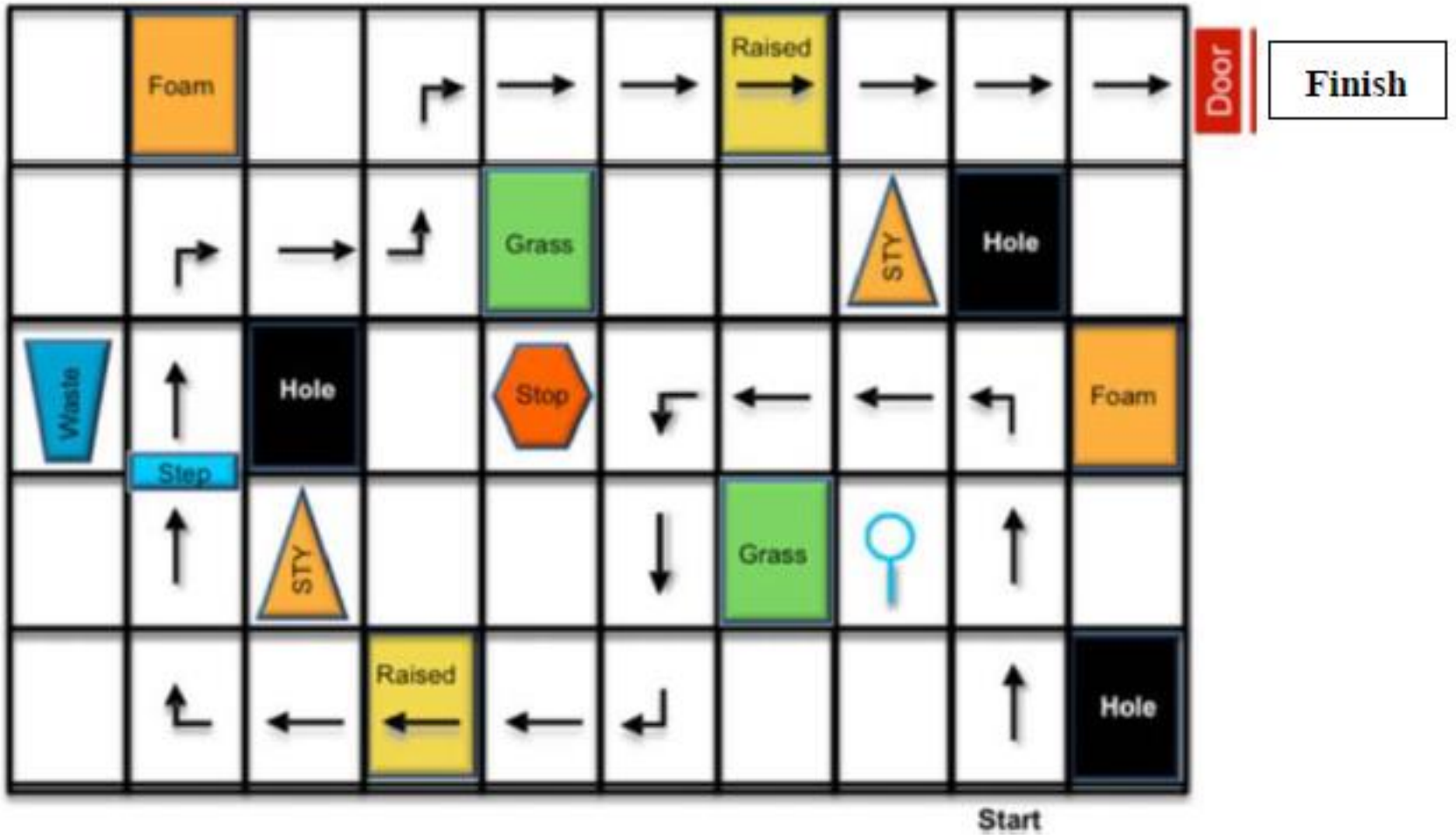
*Source: 42 U.S.C. § 1395w-104(b)(3)(G)(iv) (2018).



tisagenlecleucel
(Kymriah)

*HSCT = hematopoietic stem cell transplant

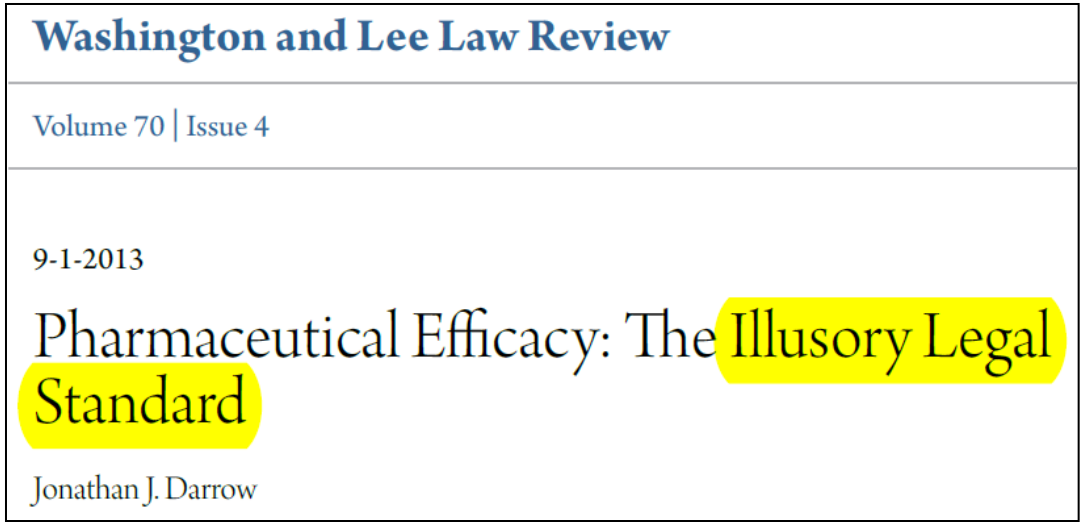
voretigene neparvovec (Luxturna)



Conclusion

- Less evidence required for FDA approval
- “Guaranteed” payment, keyed to FDA approval
- No price limits
- Poor understanding of FDA efficacy standard

Prediction: prices will continue to increase.



PORTAL
Program on Regulation, Therapeutics, and Law

DEPARTMENT OF MEDICINE
BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL

Market- & drug development-trends potentially affecting prices

Jonathan J. Darrow, SJD, LLM, JD, MBA

Faculty, Harvard Medical School
Program on Regulation, Therapeutics, & Law (PORTAL)
Brigham & Women's Hospital

DIVISION OF
PHARMACOEPIDEMIOLOGY &
PHARMACOECONOMICS

June 13, 2018