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Drug Pricing 102

SUPPLY SIDE ISSUES

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Agenda

1. Drug development
2. Government-blessed “monopolies”
3. Facilitating Competition
4. Challenges and opportunities

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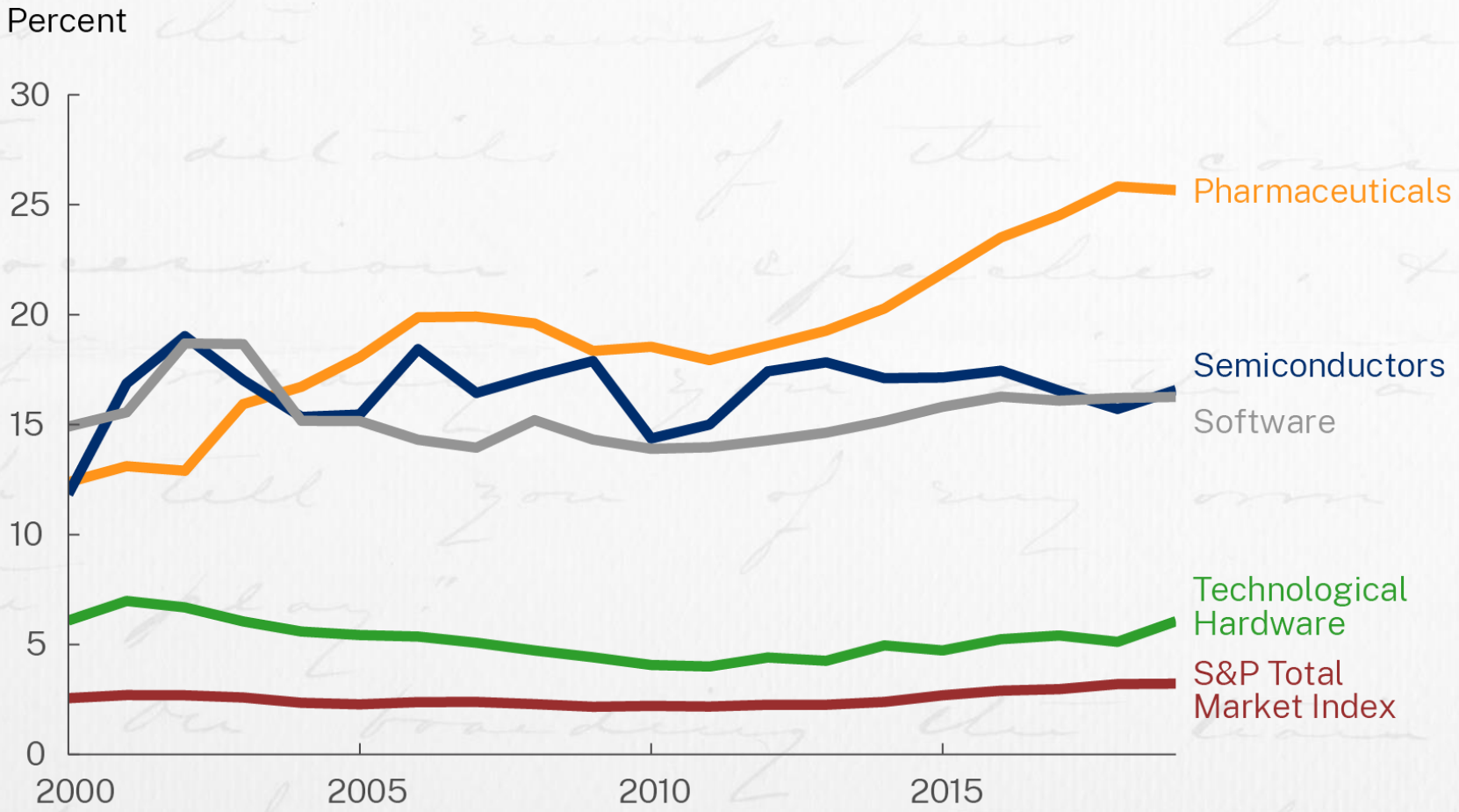
Research & development

Average R&D Intensities for Publicly Traded U.S. Companies, by Industry

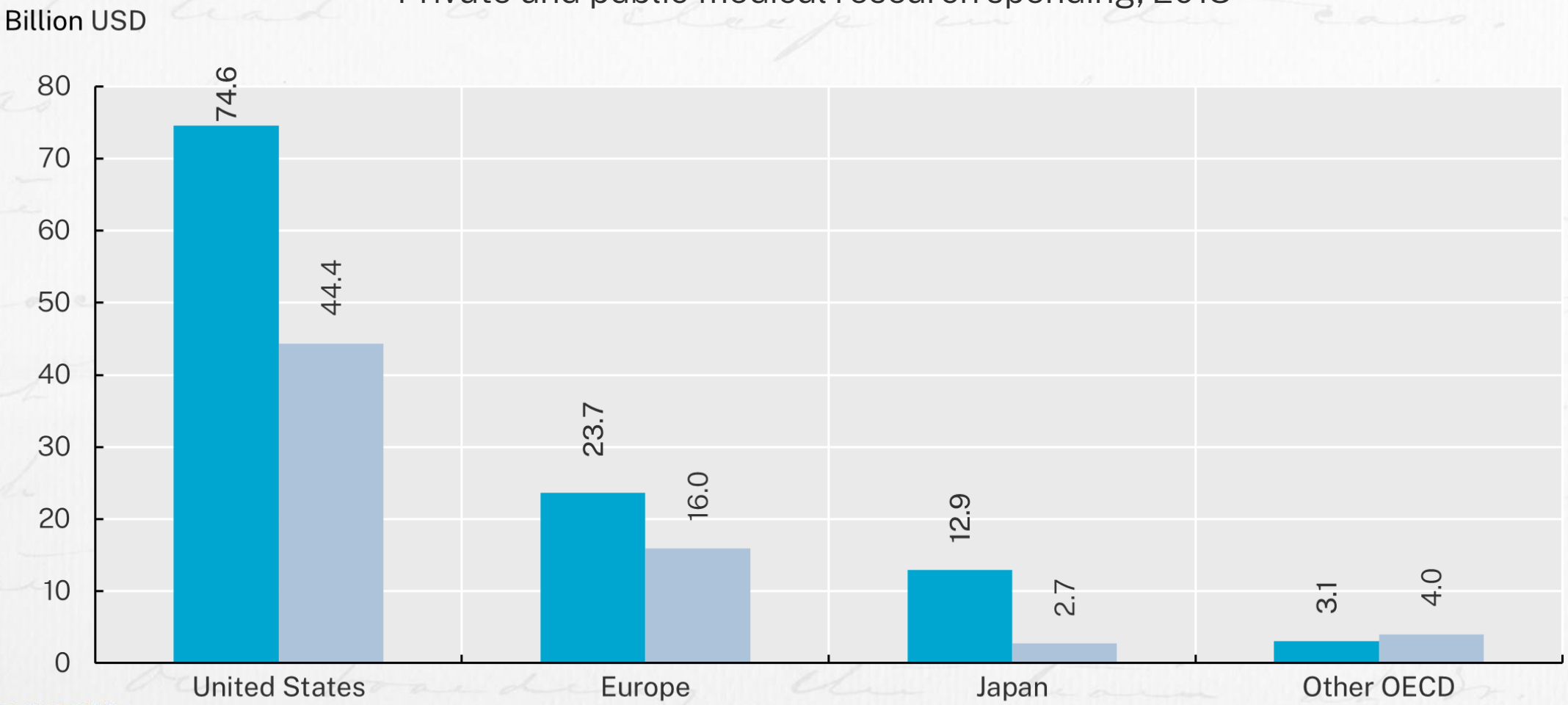


Pharmaceutical companies have devoted a growing share of their net revenues to R&D activities, averaging about 19 percent over the past two decades. By comparison, other research-intensive industries, like software and semiconductors, averaged about 15 percent.

Paragon's pet peeves

– US implicitly ***and explicitly*** funds world's research & development

Private and public medical research spending, 2018



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Paragon's pet peeves

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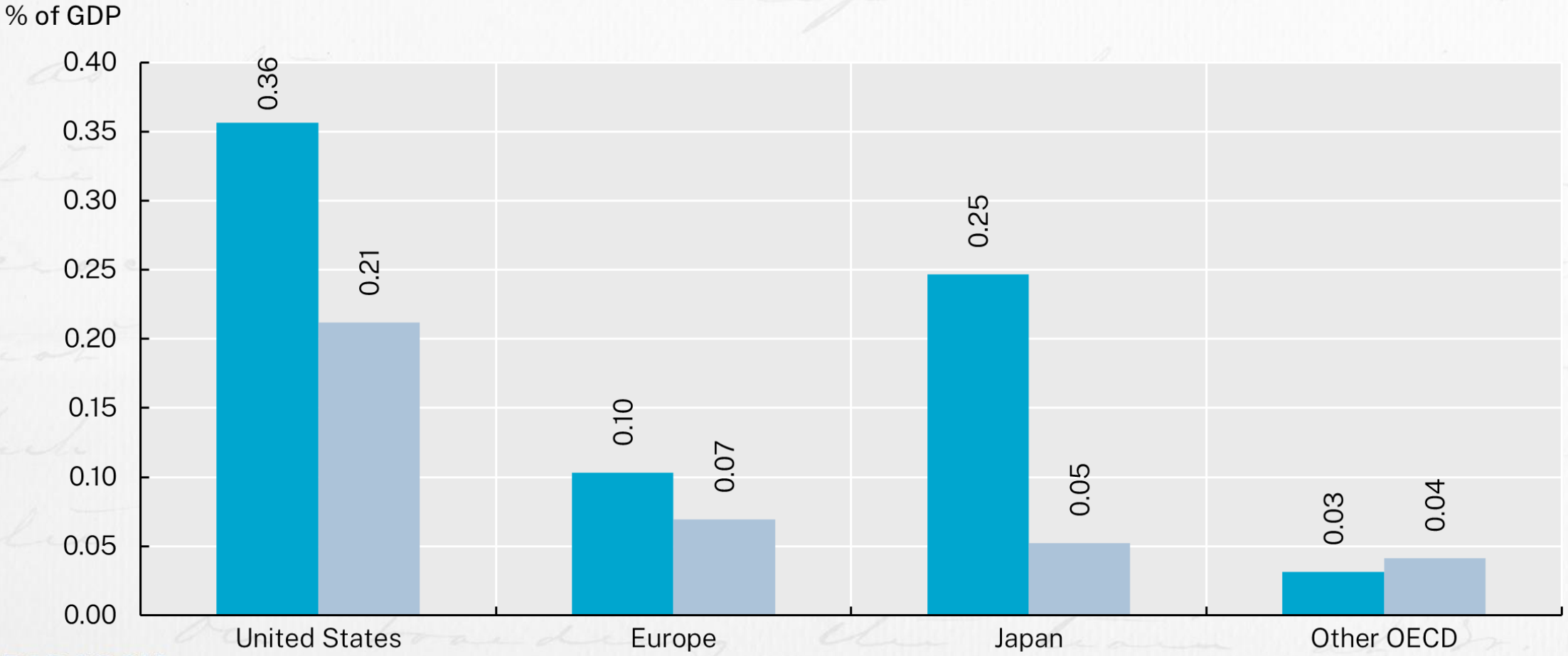

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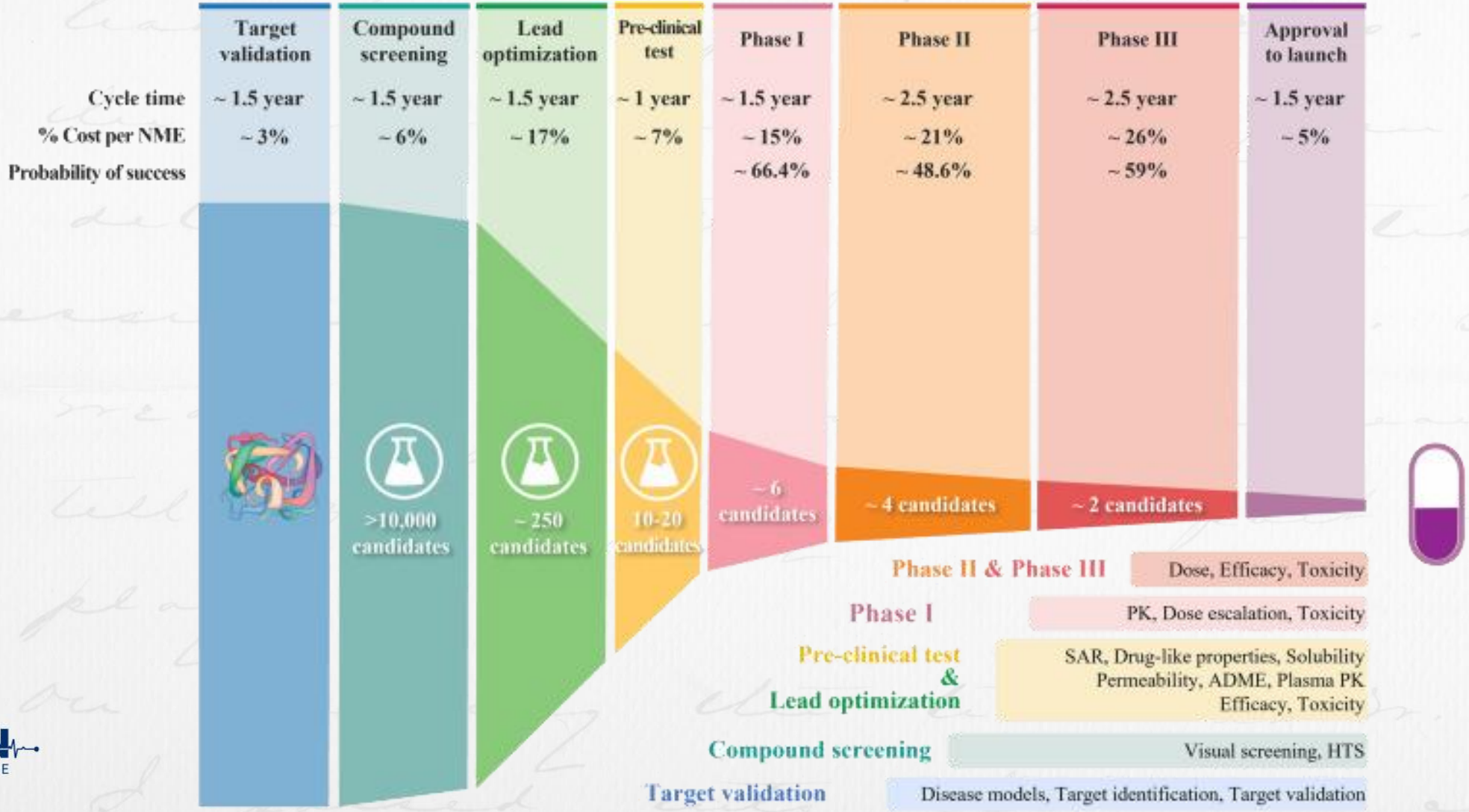
Drug Discovery, Development, and Food and Drug Administration approval — a long and arduous journey



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This process is expensive

According to the Congressional Budget Office:

*"Only about **12 percent** of drugs entering clinical trials are ultimately approved for introduction by the FDA."*

*"In recent studies, estimates of the average R&D cost per new drug range from less than $1 billion to **more than $2 billion per drug**"*

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Expedited approval pathways

Priority Review	Shortens the usual 10-month initial FDA review of new submissions to 6 months
Fast Track	Provides for more frequent communication between the FDA and the manufacturer during development and eligibility for accelerated approval and priority review.
Breakthrough Therapy	The FDA commits to intensively guide development programs beginning as early as Phase I when preliminary clinical evidence indicates a new drug for serious conditions may demonstrate substantial improvement over available therapies.
Accelerated Approval	Allows the FDA to approve a new drug based on evidence showing the drug has an effect that is “reasonably likely to predict” clinical benefit. The drug must be (1) for a serious condition and (2) provide a meaningful advantage over available therapies, and the manufacturer must agree to post-approval studies to confirm clinical benefit.

Tools to improve time and cost of R&D

Innovative Trial Approaches	Innovations in trial design can reduce time and cost (e.g., platform and basket trials, model-informed drug development, Bayesian techniques)
AI Tools	AI tools are emerging that can improve development (e.g., more efficient identification of promising drug candidates and optimizing clinical trial design)
Real-World Evidence	There have been significant improvements in our ability to study real-world data sources (e.g., de-identified medical records and insurance claims) to develop reliable and transparent evidence of safety and effectiveness, and to learn more about under-studied populations
Outcome Measurement	Innovations in what gets measured to tell if a drug is working (e.g., biomarkers, novel endpoints) can lead to more efficient clinical trials

Agenda

1. Drug development
2. Government-blessed “monopolies”
   - Patent protection & market and data exclusivity
   - Not quite a monopoly → branded competition and “me too” drugs
3. Facilitating Competition
4. Challenges and opportunities

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Innovation vs. Competition

Two competing policy goals:

Incentives to invest substantial $$ to develop new products and improve existing products

Market competition that can lead to lower prices

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Government blessed "monopolies"

United States Patent Office

Patents

- Granted to ideas that are ***novel***, ***nonobvious***, and ***useful***
- Public domain
- Protects invention for 20 years
- Multiple patents can be filed to one drug

Food and Drug Administration

- **Data exclusivity –** prohibits a competitor from utilizing the data used by the innovator product to prove its safety and effectiveness
- **Marketing exclusivity –** prohibits a competitor from coming to market even if they have run trials to generate their own data

• New small molecule	5 years data exclusivity
• Changes that require clinical trials	3 years additional data exclusivity
• New large molecule	12 years marketing exclusivity
• Orphan indication	7 years marketing exclusivity
• Qualified infectious disease product	5 years additional marketing exclusivity
• Qualified pediatric trials	6 months additional marketing exclusivity
• New small molecule generic	180 days marketing exclusivity

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Government blessed "monopolies"

Patent =
20 years*

Drug dvlp ≈
13.5 years

Small molecule data exclusivity = 5 years

Orphan drug market exclusivity = 7 years

Biologic market exclusivity = 12 years

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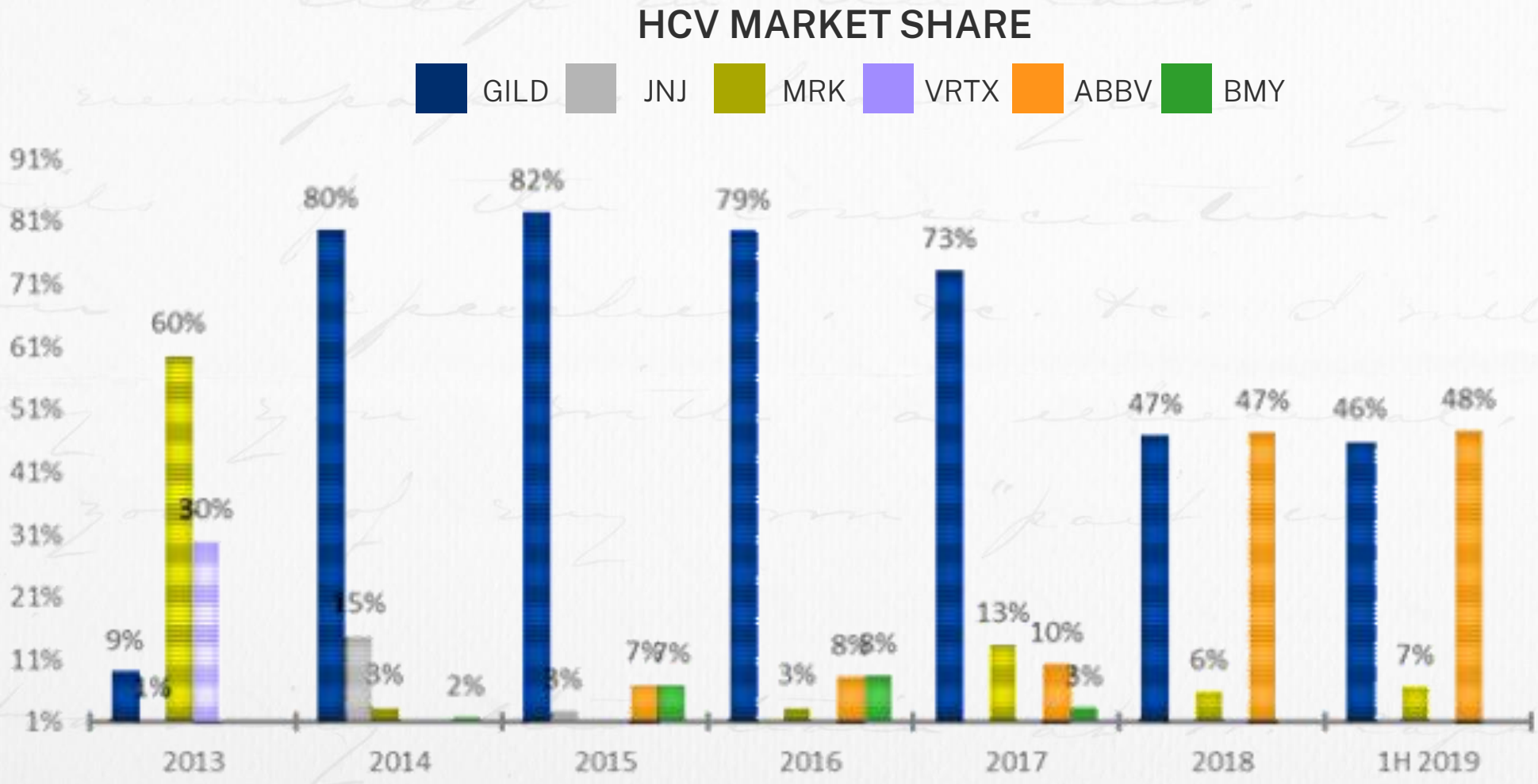
*Plus up to 5 years patent term extension to compensate for time in testing and regulatory review

Government-blessed "monopolies"

- Brands can face competition from other brands
- Unfairly derided as "**me too**" drugs
- Case study: Hepatitis C
- Competitor around 1/3 price of innovator



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Hatch-Waxman Act and generics

- The *Drug Price Competition and Patent Term Restoration Act* of 1984 is commonly referred to as "Hatch-Waxman" after its primary sponsors
- **Expedited approval** – created "Abbreviated New Drug Application" that only requires proof generic is bioequivalent (no clinical trials needed to prove safety and efficacy)
- **Patent challenges** – creates a process to resolve patent disputes
- **Patent term extensions** – creates a process to extend patent life to compensate for regulatory review
- **Regulatory exclusivity** – creates new market exclusivities, including brand exclusivities as well as a reward of 180-days of marketing exclusivity for first generic to successfully challenge a patent

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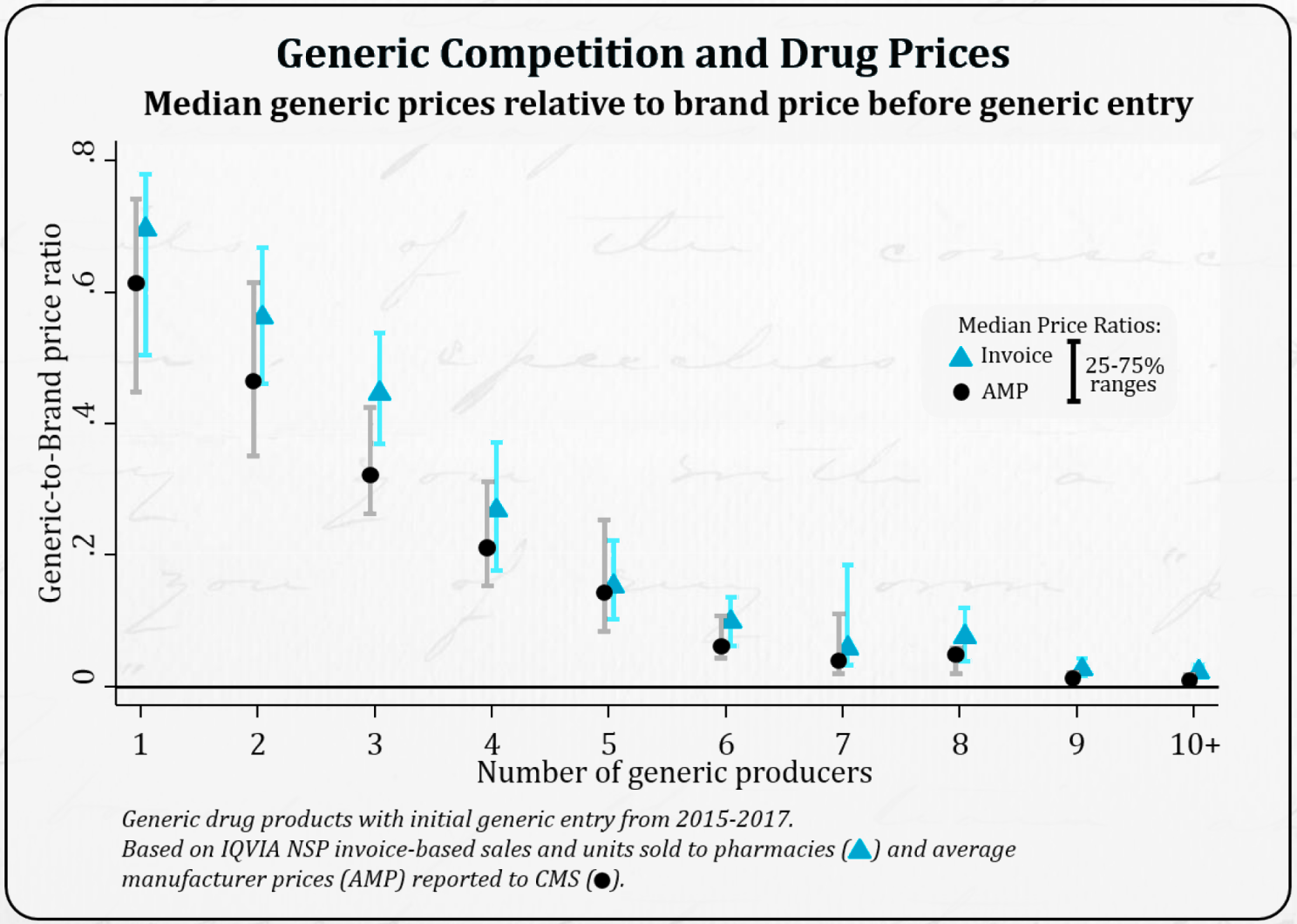
Generic competition is very effective at lowering net prices



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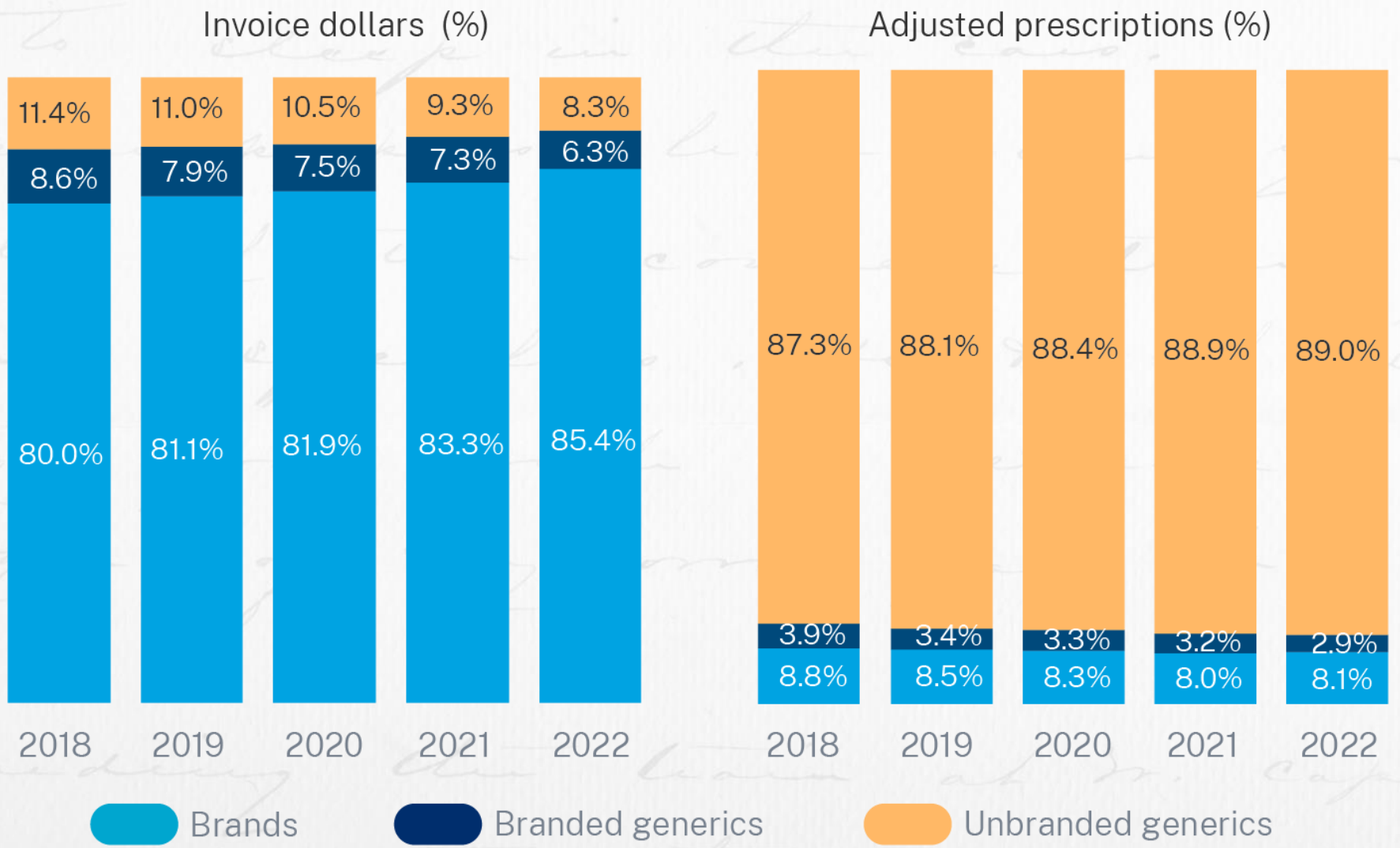
Hatch-Waxman Act and generics

- The U.S. both pays less for generics and uses more of them compared to other OECD nations.
  - About 84% of all prescription volume in the U.S. is generics compared to 35% in other OECD nations.
  - The U.S. pays about $0.84 on the dollar for generic drugs compared to other OECD nations.



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Biologics Price Competition and Innovation Act and biosimilars

- *Biologics Price Competition and Innovation Act* passed as part of the Affordable Care Act in 2010
- **Expedited approval** – Created a new abbreviated application for "biosimilars"
- **"Patent dance"** – Created a framework for addressing issues of patent infringement that sets timeline for notification, response, analysis, and litigation
- **Interchangeability** – A pharmacist can't substitute a biosimilar for a biologic without re-consulting the prescribing physician unless FDA has determined that the products are "interchangeable" (e.g., based on a "**switching study**")

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Generic Drugs vs. Biosimilars

Generic Drugs

- Follow-on products for small molecule drugs
- Must be the “same” as the reference brand product, including same active ingredient
- A generic can rely on the brand drug’s approval to show safety and effectiveness, as long as it’s “bioequivalent” to the brand
- Can be substituted for the brand drug at the pharmacy, without re-consulting the physician

Biosimilars

- Follow-on products for larger, more complex biologics
- Must be “higly similar” to the reference biologic with no “clinically meaningful” differences
- Products that meet this standard can rely on the brand product’s approval
- Can not be substituted for the reference product at the pharmacy, unless the product has an additional approval as “interchangeable”

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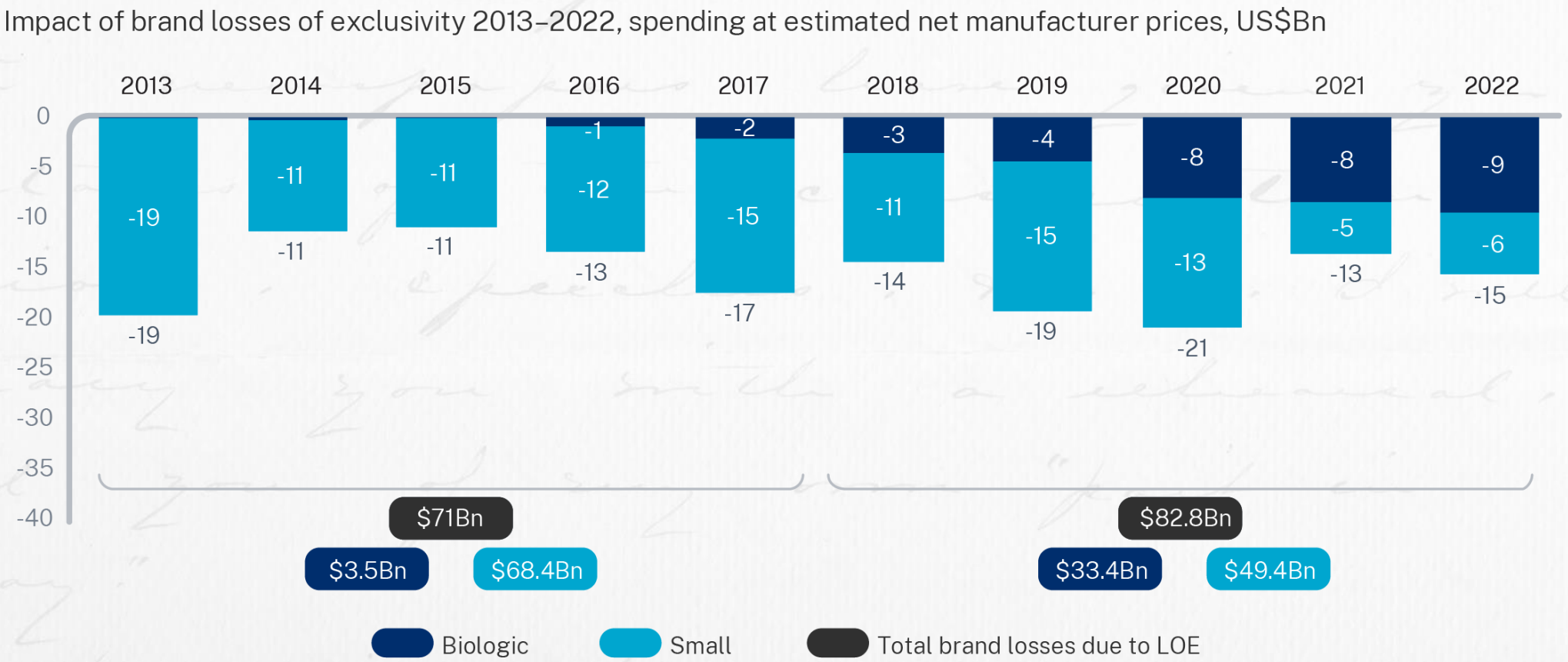
Biologics Price Competition and Innovation Act and biosimilars

- Competition for biologics has been slow coming
- Additional standard to meet for pharmacy substitution–interchangeability
- Starting to see impact in last three years



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Impact of **Inflation Reduction Act** on these dynamics

Medicare price "negotiation" is expected to impose significant price caps, beginning as soon as 9 years after approval for drugs, 13 years after approval for biologics

A few potential impacts:

- Changed Incentives for Generic/Biosimilar Entry: price cuts could make market entry less profitable for follow-on products, but potentially more attractive for brands (because products are not subject to "negotiation" after generic/biosimilar entry
- Changed Incentives for Product Development: could skew development from drugs to biologics, and away from products with use predominantly in Medicare populations
- Changed Incentives for Post-Market Innovation: could alter incentives for post-market innovation (e.g., new indications for approved products)

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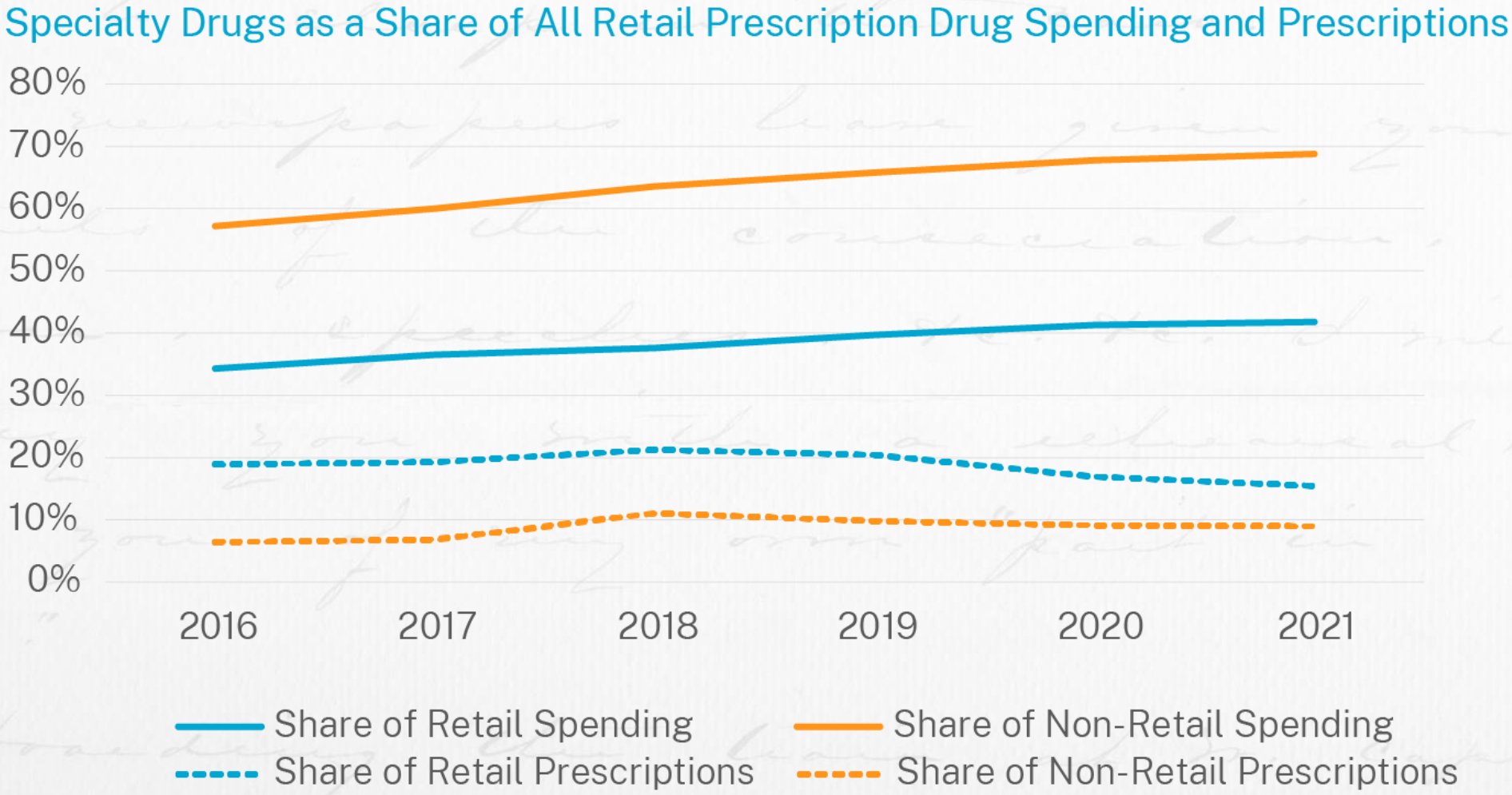
Rise of specialty medications

Specialty drugs may:

- Treat chronic, complex, often rare conditions
- May require special handling (specialty pharmacies)
- May require patient monitoring
- *Expensive* - $6,000 or much more



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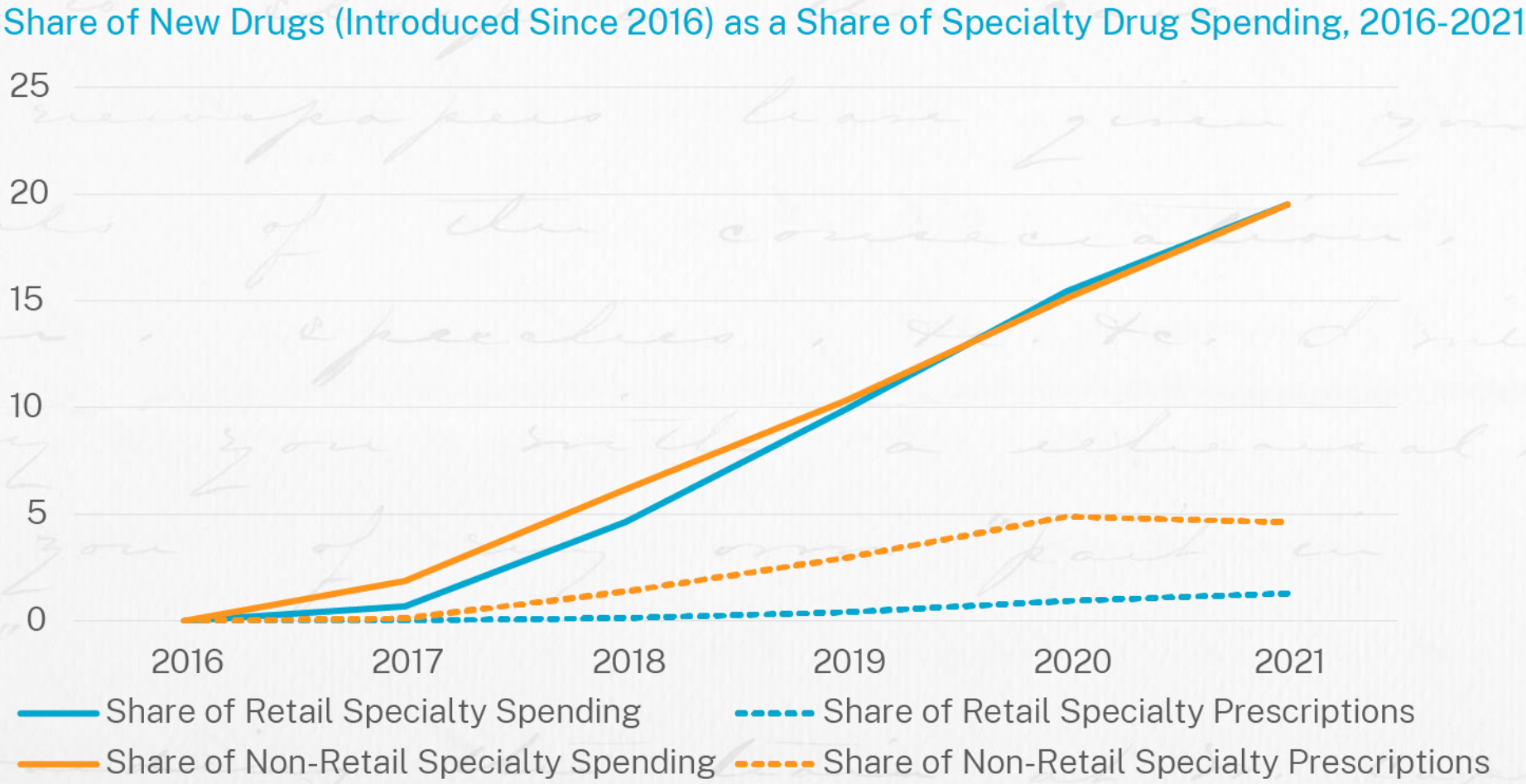
Rise of specialty medications

- Growing share of drug market
- Trend expected to continue



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Rise of specialty medications

- **Possible causes:**
  - Scientific development – e.g. unlocking the secrets of the genome
  - Regulatory regime – Orphan Drug Act
  - Reimbursement – generosity of Part B
- **Challenges:**
  - Higher out-of-pocket
  - Stress on reinsurance
  - Different distribution channels

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“Lifecycle management”?

- **Patent thickets:** a large number of patents for a product (often of differing degrees of validity) that can make it highly complicated for a generic or biosimilar to enter in a timely way
- **Product hopping:** practice where a manufacturer updates a drug to a new version (potentially with useful innovations) that has
- **Patent settlements:** patent litigation can be resolved through settlements that allow competition earlier than if the patents were enforced, but later than if they weren’t
- **Orphan Drug Act:** creates exclusivity system to incentivize development of drugs for rare diseases that might otherwise not attract investment

Bayh-Dole Act and "March-in Rights"

- **Original Intent:** Enacted to spur transfer of publicly-funded intellectual property to the commercial actors
  - Prior, only 5% of government owned patents were ever commercialized
  - Passed in 1980, Bayh-Dole allows businesses and nonprofits to retain title to any federally funded inventions as long as they commit to commercialization of the invention
- **March-in Rights:** Gov't retains the ability to grant licenses for patents that resulted from federally funded R&D under certain circumstances
  - Never been exercised
  - NIH has stated authority does *not* extend to high drug prices

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Bayh-Dole Act and "March-in Rights"

- Scope is also often mischaracterized
- Most NIH funded research is basic research that does not immediately produce patents with commercial use
- Bayh-Dole applies to a "subject invention"
- Studies reveal 8-11% of new medicines are covered by even a single patent funded by a government entity

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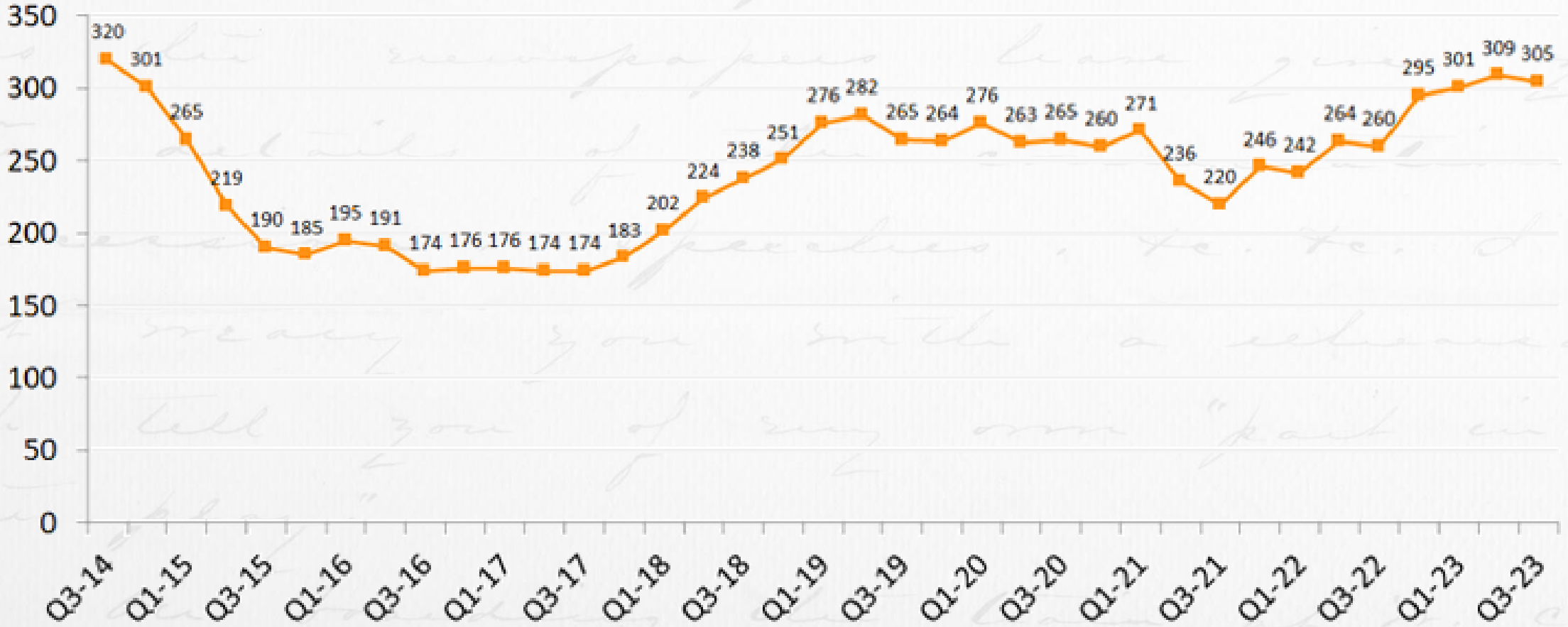
National drug shortages

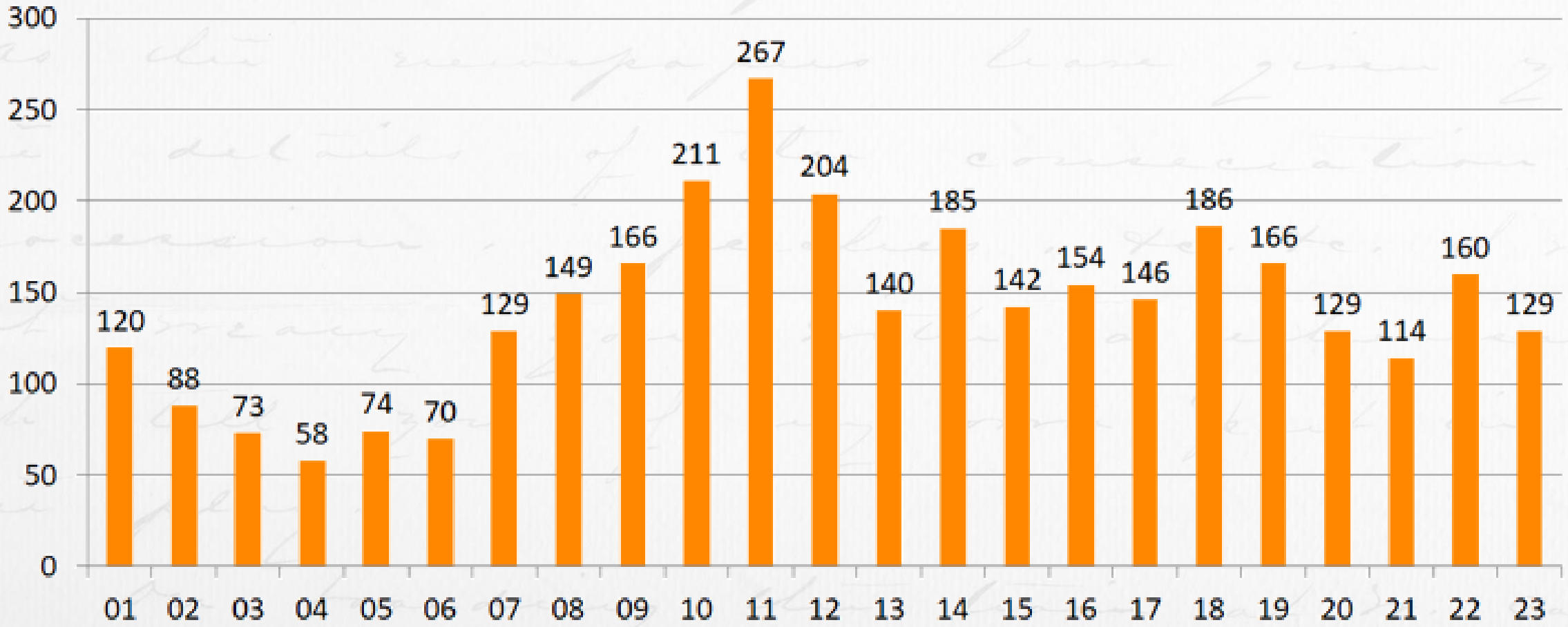
Active Shortages by Quarter — 10-Year Trend



Note: Each point represents the number of active shortages at the end of each quarter.

National drug shortages

New Drug Shortages by Year — January 2001 to June 30, 2023



Note: Each column represents the number of new shortages identified during that year.

Drug shortages

Market failure		Government failure
• Intense competition pushes prices very low • Consolidated purchasers (group purchasing organizations) reduce number of opportunities to win contracts • Supply chains migrate to lowest cost environment (often abroad) • Information assymmetry — little market insight into which products may be at risk (e.g., due to poor quality control)	or	• Acute event precipitating shortage often FDA inspection of facility that uncovers a quality issue (example: cisplatin) — can these be detected ealier or with less disruption? • High barriers to entry for new competitors, new facilities, or even new production lines • Existing government price controls do not respond, or respond slowly, to changing market dynamics

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