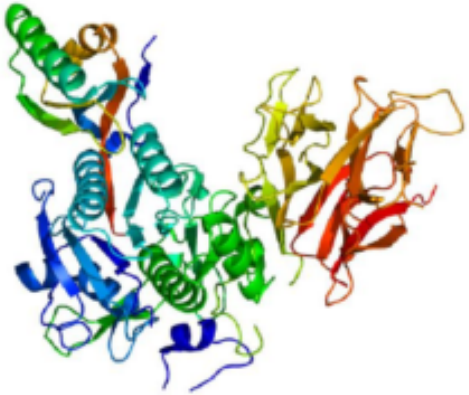
Biologics & Biosimilars: Hot Topics

February 5, 2025

NYIPLA Event at Orrick, Herrington & Sutcliffe LLP

Amgen & Section 112 Updates

Amgen v. Sanofi (S. Ct. 2023)


PCSK9

"Amgen has failed to enable all that it has claimed."

Amgen's "roadmap" and "conservative substitution" approaches "amount to little more than ***two research assignments***" that leave scientists "forced to engage in 'painstaking experimentation' ***to see what works***. That is not enablement … it is a 'hunting license.'"

"Amgen offers persons skilled in the art little more than advice to engage in 'trial and error.'"

Amgen v. Sanofi (S. Ct. 2023)

"That is not to say a specification always must describe with particularity how to make and use every single embodiment within a claimed class."

"[D]isclosing [a] general quality may reliably enable a person skilled in the art to make and use all of what is claimed, not merely a subset."

"Nor is a specification necessarily inadequate just because it leaves the skilled artist to engage in some measure of adaptation or testing."

USPTO Guidelines (January 2024)

"In Amgen, the Supreme Court, in a unanimous decision, affirmed *Sanofi-Aventisub*."

"[C]onsistent with the Federal Circuit in *Sanofi-Aventisub* and in post-*Amgen* enablement decisions, ***the Wands factors***, which were used by the USPTO prior to *Amgen*, ***will continue to be used*** to assess whether the experimentation required by the specification to make and use the entire scope of the claimed invention is reasonable."

"Federal Circuit precedent applying the *Wands* factors prior to *Amgen* is still informative as to how to *Wands* factors should be analyzed in different situations."

OssiFi-Mab v. Amgen (pending D. Mass.)

- Claims method of increasing bone density by administering Sclerostin antibodies and antiresorptive drugs.

- U.S. Patent No. 8,877,196, Claim 1:

> A method of increasing bone density in a mammalian patient in need thereof, comprising the steps of:
>
> > systemically administering to a said mammalian patient a therapeutic comprising an effective amount of a Sclerostin antagonist sequentially with an antiresorptive drug, said Sclerostin antagonist comprising an ***antibody or FAB fragment specifically binding a peptide*** selected from the group consisting of SEQ ID NOS:2-13, 22 and 23,
> >
> > wherein the antibody interferes with Sclerostin's ability to bind to LRP, thereby systemically increasing bone density.

OssiFi-Mab v. Amgen (D. Mass.)

- "The Asserted Patents [] ***attempt to lay claim over the use of a vast genus of anti-sclerostin antibodies, which are not claimed by structure but by their function*** … The specification falls far short of demonstrating to a skilled person that the inventor possessed the full scope of such antibodies and fails the enablement standard."

- "The patent is on a method of treatment involving ***a genus of perhaps millions of antibodies***."

**Amgen's statements in the Statement of Case and at Markman oral argument.*

OssiFi-Mab v. Amgen (D. Mass.)

- "***But even today***, and more so at the priority date, ***one couldn't simply snap one's fingers to make an antibody***."

- "What ***I end up with*** at the end is literally ***tens of thousands or hundreds of thousands or millions of antibodies*** from a mouse. I can then experiment with them and see whether any of them do the thing I want them to do. And I may find out that none of them does. I may find out that one or two of them do. ***And I may, if I'm very, very lucky, end up with a therapeutic treatment***."

**Amgen's statements at Markman oral argument.*

Lindis v. Amgen (D. Del. 2024)

- Claims method of reducing the non-specific release of at least one cytokine by administering “at least one bispecific immunostimulating antibody directed against a tumor antigen and a CD marker” wherein “the tumor antigen is CD19, and the CD marker is CD3.”
- Amgen’s SJ motion of no WD for functionally-defined genus claims was denied.
- On December 17, 2024, a jury found that Amgen’s BLINCYTO, a BiTE that targets CD19 and CD3, infringed Lindis’s patents.
- Jury did not find patents invalid for lack of WD or enablement.
- ***Jury awarded $50,306,120.00.*** And found Amgen’s infringement to be willful.

Lindis v. Amgen (D. Del. 2024)

- "Each of the asserted claims of the '158 patent [] recites a ***functionally-defined genus of bispecific antibodies*** (*i.e.*, antibodies defined not by their structure, but by their functional properties)."

- "The specification ***lacks any description of any structural features corresponding to the recited biological functions of binding CD19 or CD3***, being immunostimulatory, or causing non-specific release of cytokines, much less any commonalities in such structural features that might tie together a genus of such molecules."

- "The specification ***lacks any disclosure of an amino acid sequence***, which dictates the structure and function of any antibody."

**Amgen's Summary Judgment briefing.*

Lindis v. Amgen (D. Del. 2024)

- "***That the specification recites the antibodies are bispecific antibodies or bispecific scFv antibodies is not sufficient to allow a POSA to 'visualize or recognize' members of the claimed genus***. That is because not all bispecific antibodies or bispecific scFv antibodies bind to both CD19 and CD3 and meet the other functional features of the claims."
- "***Testing of countless bispecific antibodies and scFv bispecific antibodies would therefore have been necessary*** to determine which antibodies bind both tumor antigen CD19 and CD marker CD3 and perform the other functions required by the claims."

**Amgen's Summary Judgment briefing.*

Supernus v. Torrent (D.N.J. 2024)

ONCE-A-DAY FOR MIGRAINE PREVENTION
Trokendi XR®
(topiramate) extended-release capsules

- Claims sustained release formulations having an extended-release topiramate-containing component and achieving a specific plasma concentration.
- U.S. Patent No. 8,992,989, Claim 14:

> ***A sustained release formulation of topiramate*** comprising topiramate as an active ingredient, which is released immediately and continuously upon administration from the formulation, the formulation comprising:
> (a) an extended release (XR) topiramate-containing component, …
> (b) an immediate release (IR) topiramate-containing component comprising:
> (i) a complexing agent … and/or, (ii) an enhancing agent … wherein the XR component exhibits a maximum plasma concentration of topiramate in vivo at 16 or more hours after a single initial dose.

Supernus v. Torrent (D.N.J. 2024)

- The court assessed the *Wands* factors and distinguished *Amgen* in two ways:

  - The patents "***do not claim an 'entire genus'*** of release-controlling coatings regardless of physical characteristics or chemical properties. They claim sustained release formulations of topiramate comprising an XR component with cellulosic or acrylic polymers."
  - The patents "***do not require 'painstaking experimentation to see what works***.'"

**Decision is on appeal and fully briefed.*

Biosimilars & IRA

Biosimilars & IRA

Eligible Drugs	Ineligible Drugs
• Selected from top 50 single source drugs with highest (over a 12-month period) total Medicare spending for each Part ➢ Part D: 2026 and 2027 ➢ Parts D and B: subsequent periods • Must have been on the market for a set number of years ➢ Small molecule: 7 years ➢ Biologic: 11 years • Must lack generic or biosimilar competition ➢ Approved by FDA and “marketed” ➢ Selection of biologic drugs for negotiation can be delayed by up to two years if a biosimilar product is likely to enter the market in that time	• “Small biotech drugs” through 2028 • Drugs with Medicare spending of less than $200M in 2021 (increased for subsequent years) • Drugs with one orphan designation and that are FDA-approved for only that indication • Plasma-derived products • Drugs administered in hospitals (Part A drugs)

Biosimilars & IRA

Qualifying Single Source Drug

- IRA defines a Qualifying Single Source Drug (QSSD) as approved under an NDA or BLA and marketed pursuant to such approval.
- CMS's guidance is more expansive than the statutory language.
- Guidance defines QSSD to include "all dosage forms and strengths" of *any* drug marketed by the manufacturer "with the same active moiety":

  "**all dosage forms and strengths of the drug with the same active moiety and the same holder of a NDA, inclusive of products that are marketed pursuant to different NDAs**."

- Guidance expands the universe of products available for selection earlier.
- It shortens the period to recoup investment for newer drugs that share an active moiety with an earlier-approved drug.

Biosimilars & IRA

Bona Fide Marketing

- IRA exempts drugs that have a generic/biosimilar competitor on the market.
- IRA requires that the generic/biosimilar competitor is "***approved***" and "***marketed***."
- CMS's guidance expands this definition.
- It states that a generic or biosimilar must have been the subject of "***bona fide marketing***."
- Whether "bona fide marketing" has occurred is a "holistic inquiry" based on the "totality of the circumstances."
- CMS states that without a provision for "bona fide marketing," a generic or biosimilar maker could launch a token or de minimis amount of drug.

Biosimilars & IRA

First Ten Drugs

Drug	Manufacturer	Drug Type	List Price 2023*	Negotiated Price 2026*
1. Enbrel (1998)	Amgen	Biological Product	$7,106.00	$2,355.00
2. Fiasp (2000)	Novo Nordisk	Biological Product	$495.00	$119.00
3. Januvia (2006)	Merck	Small Molecule	$527.00	$113.00
4. Stelara (2009)	Janssen	Biological Product	$13,836.00	$4,695.00
5. Xarelto (2011)	Janssen / Bayer	Small Molecule	$517.00	$197.00
6. Eliquis (2012)	BMS	Small Molecule	$521.00	$231.00
7. Imbruvica (2013)	PCYC / Janssen	Small Molecule	$14,934.00	$9,319.00
8. Farxiga (2014)	AstraZeneca	Small Molecule	$556.00	$178.00
9. Jardiance (2014)	Boehringer	Small Molecule	$573.00	$197.00
10. Entresto (2015)	Novartis	Small Molecule	$628.00	$295.00

**30-day supply*

Biosimilars & IRA

Next Fifteen Drugs (January 17, 2025)

Drug	Manufacturer	Drug Type	Total Prescription Drug Costs (November 2023–October 2024)
1. Ozempic / Rybelsus / Wegovy (2017)	Novo Nordisk	Small Molecule	$14.4B
2. Trelegy Ellipta (2017)	GSK	Small Molecule	$5.1B
3. Xtandi (2012)	Astellas / Pfizer	Small Molecule	$3.2B
4. Pomalyst (2013)	BMS	Small Molecule	$2.1B
5. Ibrance (2015)	Pfizer	Small Molecule	$2.0B
6. Ofev (2014)	Boehringer	Small Molecule	$2.0B
7. Linzess (2012)	AbbVie	Small Molecule	$1.9B
8. Calquence (2017)	AstraZeneca	Small Molecule	$1.6B

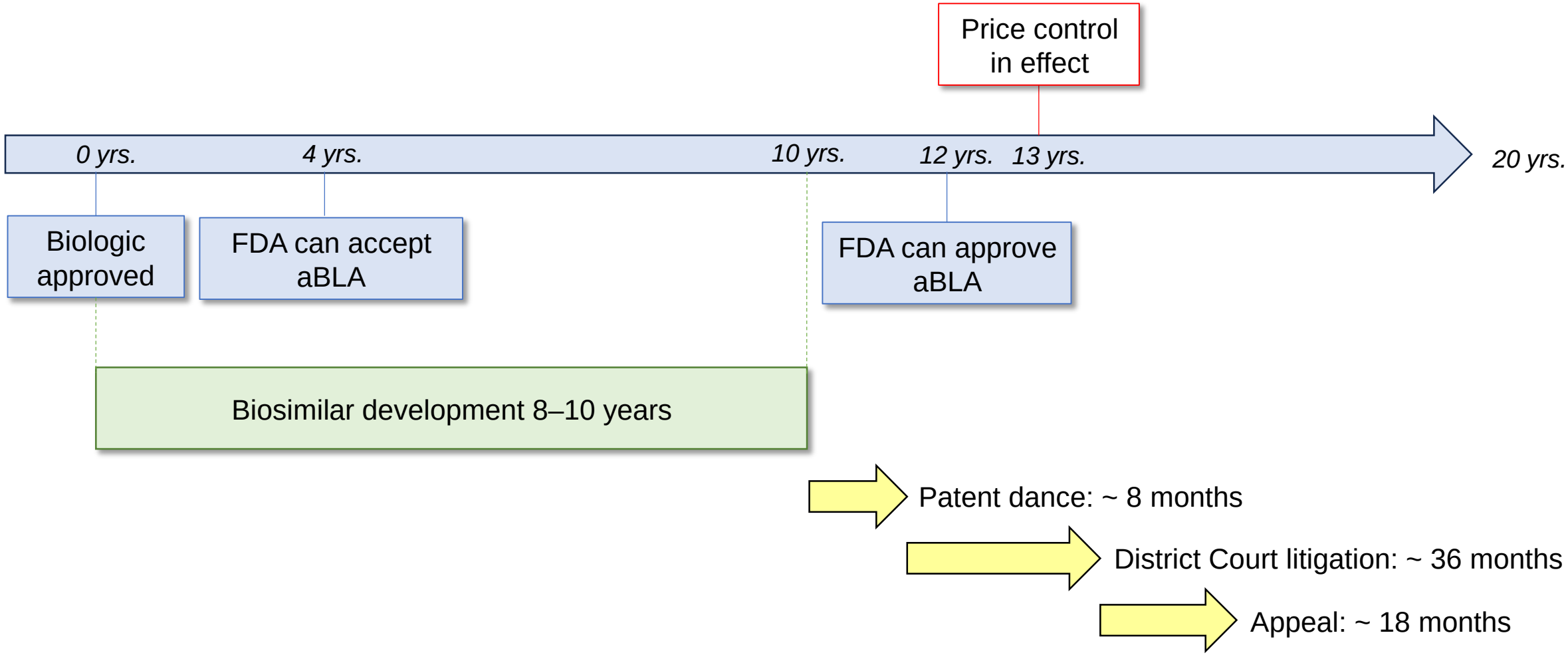
Biosimilars & IRA

Next Fifteen Drugs (January 17, 2025)

Drug	Manufacturer	Drug Type	Total Prescription Drug Costs (November 2023–October 2024)
9. Austedo / Austedo XR (2017)	Teva	Small Molecule	$1.5B
10. Breo Ellipta (2013)	GSK	Small Molecule	$1.4B
11. Tradjenta (2011)	Boehringer / Lilly	Small Molecule	$1.1B
12. Xifaxan (2004)	Bausch / Salix	Small Molecule	$1.1B
13. Vraylar (2015)	AbbVie	Small Molecule	$1.1B
14. Janumet / Janumet XR (2007)	Merck	Small Molecule	$1.1B
15. Otezla (2014)	Amgen	Small Molecule	$1.0B

Biosimilars & IRA

BPCIA Interplay



IRA Lawsuits

IRA Lawsuits

Lawsuits challenging constitutionality of IRA and/or alleging APA violations:

- Merck (Januvia) – D.D.C.
- AstraZeneca (Farxiga, Lynparza, Calquence, Soliris) – D. Del.
- Boehringer Ingelheim (Jardiance) – D. Conn.
- Novartis (Entresto) – D.N.J.
- Novo Nordisk (Novolog, among others) – D.N.J.
- Janssen (Xarelto) – D.N.J.
- Bristol Myers Squibb (Eliquis and Opdivo) – D.N.J.
- Astellas (Xtandi and Myrbetriq) – N.D. Ill.
- National Infusion Center Association, PhRMA, GCCA (identified PhRMA member products) – W.D. Tex.
- Dayton Area Chamber of Commerce, Ohio Chamber of Commerce, Michigan Chamber of Commerce, U.S. Chamber of Commerce (identified member's (AbbVie) Imbruvica) – S.D. Ohio
- Teva (QSSD and "Bona Fide Marketing" violate APA) – D.C.

IRA Lawsuits

Fresenius Amicus Brief

"[I]nnovation is critical to the future of our society, and the pharmaceutical industry cannot survive without it…. The regulatory scheme at issue …, however amounts to arbitrary price controls, which may be intended to reduce prices but actually reduce generic and biosimilar bioavailability. ***The price controls undermine incentives for companies to develop new drug products as well as for competitors to develop and provide generic and biosimilar alternatives, and generic and biosimilar medicines provide more effective and more sustainable reductions in drug prices than the Inflation Reduction Act ('IRA')***."

IRA Lawsuits

Teva Amicus Brief

"The IRA steamrolls the market incentives on which the BPCIA relies."

"Although the IRA formally excludes products that already face generic and biosimilar competition from the Program, the statute creates a race between CMS and follow-on competitors that ***the generic and biosimilar industries will almost invariably lose***."

IRA Lawsuits

Teva Amicus Brief

"Because the IRA authorizes CMS to select a biologic for the price-control program after 11 years, ***biosimilar manufacturers have no chance to get onto the market before the highest-value biological products are selected***."

"The period between selection of a drug and the end of negotiations is only 9 months…. CMS requires biosimilars or generics to prove 'bona fide marketing' before the end of that 9-month period. For biosimilar manufacturers targeting biologics selected for IRA negotiations 11-12 years after initial approval, beating the negotiation deadline is impossible."

IRA Lawsuits

AstraZeneca Lawsuit

- Judge Connolly held that AstraZeneca's claim that its Fifth Amendment due process rights were violated fails as a matter of law since the IRA is not a gun to the head but instead "a powerful incentive—the opportunity to sell products to more than 49 million Medicare and Medicaid beneficiaries—to induce drug manufacturers to participate in the Program and negotiate with CMS maximum fair prices for selected drugs."

- According to Judge Connolly, the IRA's drug price negotiation is "a potential economic opportunity that AstraZeneca is free to accept or reject."

- And because "AstraZeneca's participation in Medicare is not involuntary, ***AstraZeneca does not have a protected property interest in selling drugs to the Government at prices the Government will not agree to pay***."

IRA Lawsuits

District Court

- Teva (D.C.) – QSSD and “Bona Fide Marketing” violate APA
  - Case update: newly filed January 2025
  - Teva argues that CMS’s guidance violates the APA and the due process clause of the Fifth Amendment

- National Infusion Center Association, PhRMA, GCCA (W.D. Tex.) – PhRMA member products
  - Case update: remanded back to district court in November 2024
  - W.D. Tex. granted defendants’ motion to dismiss and the Fifth Circuit reversed; NICA filed a renewed SJ motion in January 2025

- Merck (D.C.) – Januvia
  - Case update: reply brief in support of defendants’ cross-motion for SJ filed November 2023
  - Merck argues that the IRA takes property without just compensation in violation of the Fifth Amendment and compels speech in violation of the First Amendment

IRA Lawsuits

Pending Cases on Appeal

- AstraZeneca (Farxiga), BMS (Eliquis), and Janssen (Xarelto) (3d Cir., consolidated)
  - Case update: oral argument took place in October 2024
  - Companies argue that the IRA violates the Fifth Amendment's takings clause, compels speech in violation of the First Amendment, and imposes unconstitutional conditions on participation

- Novo Nordisk (3d Cir.) – Novolog
  - Case update: reply brief for appellants filed January 2025
  - Novo Nordisk argues that CMS's actions violate plain statutory guidelines and that IRA's price control provisions are unconstitutional

- Novartis (3d Cir.) – Entresto
  - Case update: brief of appellant filed December 2024
  - Novartis argues that the IRA violates the Fifth Amendment's takings clause, compels speech in violation of the First Amendment, and that the IRA's excessive fines violate the Eighth Amendment

IRA Lawsuits

Pending Cases on Appeal

- Boehringer (2d Cir.) – Jardiance
  - Case update: brief of appellees filed in January 2025
  - Boehringer argues that the IRA violates the Constitution and APA and that the district court erroneously rejected its claims on the theory the program is voluntary

- Dayton Area Chamber of Commerce (members including AbbVie) (6th Cir.) – Imbruvica
  - Case update: opening brief filed in December 2024
  - Chamber argues that the district court erred in dismissing claims for improper venue and should have transferred the case

BPCIA IPRs & Settlements

BPCIA IPRs

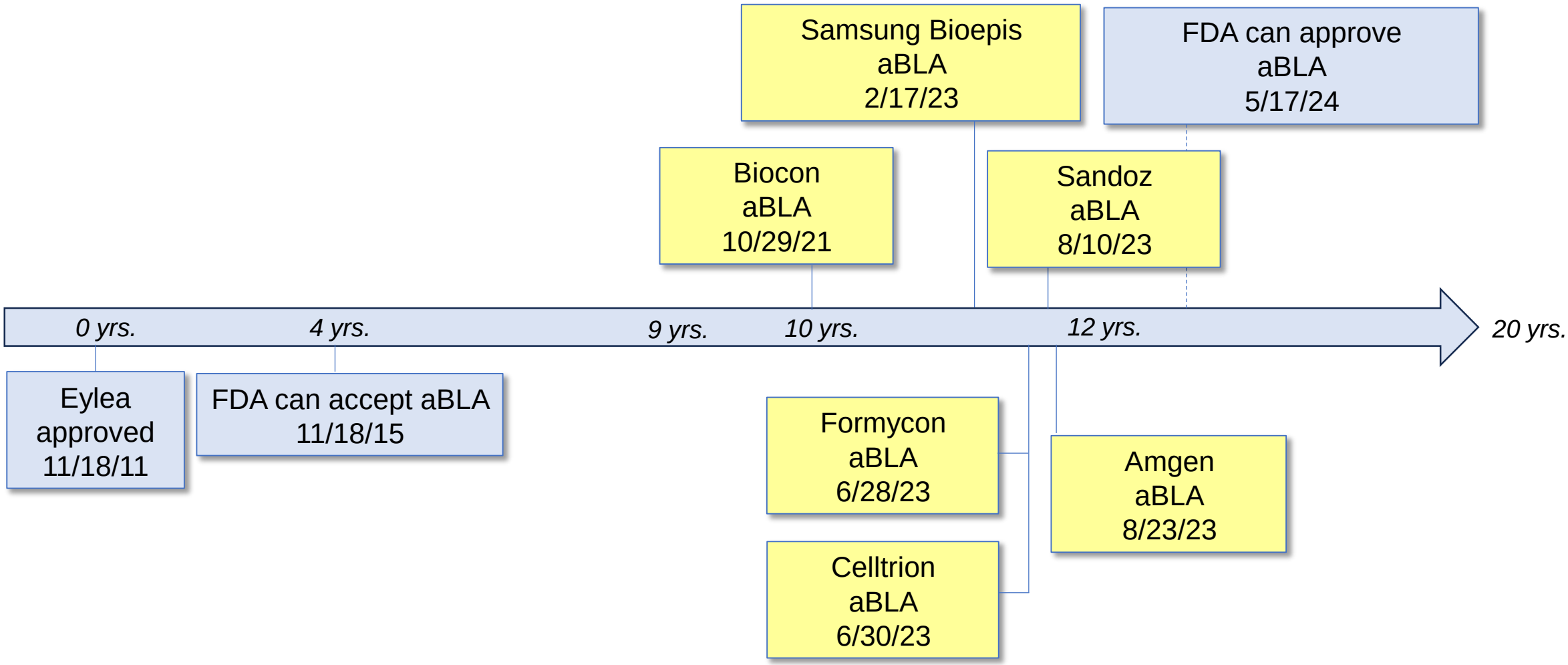
Biosimilar makers leverage IPRs to obtain settlements and avoid BPCIA.

Patent Challenger	Biologic	Biosimilar	IPR No.
Amgen	Soliris	Bkemv	IPR2019-00739
Fresenius Kabi	Actemra (toci)	Tyenne	IPR2021-01024
Mylan	Herceptin	Ogivri	IPR2016-01693

BPCIA Injunctions

BPCIA Injunctions

Timing of Filings



BPCIA Injunctions
Grants

Case	Reference Product	Biosimilar	Date of Preliminary Injunction	Date of Permanent Injunction
Amgen v. Apotex (S.D. Fla.)	Neulasta	Lapelga	12/9/15	
Immunex v. Samsung Bioepis (D.N.J.)	Enbrel	Eticovo		11/3/21
Regeneron v. Mylan/Biocon (N.D. W. Va.)	Eylea	Yesafili		6/11/24
Regeneron v. Samsung Bioepis (N.D. W. Va.)	Eylea	Opuviz	6/14/24	
Regeneron v. Formycon AG (N.D. W. Va.)	Eylea	Ahzantive	6/21/24	
Regeneron v. Celltrion (N.D. W. Va.)	Eylea	Eydenzelt	6/28/24	

BPCIA Injunctions
Denials

Case	Reference Product	Biosimilar	Date of Denial
Amgen v. Sandoz (N.D. Cal.)	Neupogen	Zarxio	3/19/15
Genentech v. Amgen (D. Del.)	Avastin	Mvasi	7/19/19
Genentech v. Amgen (D. Del.)	Herceptin	Kanjinti	7/19/19
Biogen v. Sandoz (D. Del.)	Tysarbi	Tyruko	7/20/23
Alexion v. Samsung Bioepis (D. Del.)	Soliris	Epysqli	5/6/24
Regeneron v. Amgen (N.D. W. Va.)	Eylea	Pavblu	9/23/24

At-Risk Launches

At-Risk Launches

A number of biosimilar makers have launched at-risk, including:

BPCIA Litigation	Reference Product	Biosimilar Manufacturer	Biosimilar
Amgen v. Sandoz (N.D. Cal.)	Neupogen	Sandoz	Zarxio (launched 9/3/15)
Janssen v. Celltrion (D. Mass.)	Remicade	Celltrion	Inflectra (launched 10/17/16)
Amgen v. Mylan (W.D. Pa.)	Neulasta	Mylan	Fulphila (launched 7/9/18)
Genentech v. Amgen (D. Del.)	Avastin	Amgen	Mvasi (launched 7/18/19)
Genentech v. Amgen (D. Del.)	Herceptin	Amgen	Kanjinti (launched 7/18/19)
Regeneron v. Amgen (N.D. W. Va.)	Eylea	Amgen	Pavblu (launched 10/30/24)

Thank you!

Nos. 24-1819, 24-1820, 24-1821

IN THE

United States Court of Appeals for the Third Circuit

AstraZeneca Pharmaceuticals LP, *et al*., *Appellants*,
v.
U.S. Secretary of Health & Human Services, *et al.*, *Appellees*.

On Appeal from the United States District Court
for the District of Delaware, No. 1:23-cv-931 (Connolly, J.)

Bristol Myers Squibb Co., *Appellant*,
v.
U.S. Secretary of Health & Human Services, *et al.*, *Appellees*.

On Appeal from the United States District Court
for the District of New Jersey, No. 3:23-cv-3335 (Quraishi, J.)

Janssen Pharmaceuticals Inc., *Appellant*,
v.
U.S. Secretary of Health & Human Services, *et al.*, *Appellees*.

On Appeal from the United States District Court
for the District of New Jersey, No. 3:23-cv-3818 (Quraishi, J.)

BRIEF FOR TEVA PHARMACEUTICALS USA INC. AS AMICUS CURIAE IN SUPPORT OF APPELLANTS

Alexandra Lu
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Brian T. Burgess
Matthew Wetzel
Rohiniyurie Tashima
GOODWIN PROCTER LLP
1900 N Street, NW
Washington, DC 20036
(202) 346-4000

Counsel for Amicus Curiae

July 19, 2024

Additional Counsel Listed on Inside Cover

Natasha E. Daughtry
GOODWIN PROCTER LLP
601 South Figueroa Street, Suite 4100
Los Angeles, CA 90017
(213) 426-2500

CORPORATE DISCLOSURE STATEMENT

Teva Pharmaceuticals USA, Inc. is an indirect wholly owned subsidiary of Teva Pharmaceutical Industries Ltd. No other publicly held company owns 10% or more of the stock of Teva Pharmaceutical Industries Ltd.

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INTEREST OF THE AMICUS CURIAE[1]

Amicus curiae Teva Pharmaceuticals USA, Inc. (Teva) is a leader in the supply of generic drug products to American patients. The Teva family of companies also invests hundreds of millions of dollars every year to research and develop innovative specialty and biopharmaceutical treatments to increase access and improve patients' health. Given Teva's work as both a brand-name and generic and biosimilar drug manufacturer, Teva is well positioned to address the market-distorting effects of the Inflation Reduction Act's (IRA's) Drug Price Negotiation Program, particularly as they relate to the biosimilar drug industry.

Teva submits this brief to assist the Court in understanding the IRA's market-distorting effects on the generic and biosimilar industries. Teva respectfully submits that this background is relevant to assessing the Government's assertions that participation in its price-mandating program is voluntary or that CMS can be compared to an ordinary market participant bargaining with drug manufacturers at arm's length.

[1] Counsel for all parties have consented to the filing of this brief. No party or party's counsel authored this brief in whole or in part. No party, party's counsel, or person other than *amicus curiae* and its counsel made a monetary contribution to fund the preparation or submission of this brief.

INTRODUCTION AND SUMMARY OF ARGUMENT

The "federal government dominates the healthcare market" and "uses that market power to get drug makers to subsidize healthcare." *Sanofi Aventis U.S. LLC v. U.S. Dep't of Health & Hum. Servs.*, 58 F.4th 696, 699 (3d Cir. 2023). With the IRA's Drug Price Negotiation Program (the Program), the Government has gone much further than merely wielding its market power, choosing to mandate that selected manufacturers supply drugs at significantly reduced prices and not lifting these mandated prices even when lower-cost generic and biosimilar medications are certain to launch before the mandated price will take effect. Perversely, these Government mandates that are ostensibly intended to benefit patients and bring down healthcare spending will in practice undercut competition from generic and biosimilar manufacturers, leading to a narrower and more fragile market with more risk of single-source markets and drug shortages.

As Appellants discuss, innovator drug and biological products require significant investments and great commercial risk. That is also true for generic and biosimilar manufacturers. Indeed, the average biosimilar—a follow-on of a biologic drug—costs approximately $100 to $300 million and six to nine years to develop. Miriam Fontanillo, et al., McKinsey & Co., *Three Imperatives for R&D in Biosimilars* (Aug. 19, 2022), https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars. Patients and the healthcare

system as a whole benefit enormously from generic and biosimilar competition, which helps to bring down prices while diversifying the sources for critical medicines, helping to avoid shortages. But companies will only undertake the substantial investments needed to develop and secure approval for generic and biosimilar products if there are robust market opportunities to reward their efforts.

The IRA upends the healthcare market and its incentive structure, as it directs CMS to select certain brand-name drug and biological products that must be sold at a government-dictated "maximum fair price" unless the manufacturers abandon Medicare and Medicaid patients. The market-distorting impact of this program extends far beyond the selected manufacturers themselves by also undercutting generics and biosimilars. As implemented by CMS, the agency may select drugs or biological products and impose a price cap, even if generic or biosimilar competition is forthcoming. The government-dictated price then sets the market, subjecting follow-on manufacturers to effective price caps even though they had no opportunity to participate in the putative negotiation. In fact, the IRA's discount program disadvantages generics and biosimilars in comparison to the selected innovator drug, compelling discounts that are lifted for Program participants. Nor do generic and biosimilar manufacturers have any practical ability to enter the market before the price caps are imposed, as the IRA is structured to subject brand products to potential

selection *before* the expiration of applicable exclusivity periods that block generic and biosimilar competition.

Although the IRA purports to offer relief from the maximum fair price upon generic entry, that relief is illusory. Selected brand products remain subject to the government price even after they face generic or biosimilar competition, unless and until CMS deems that there is a generic or biosimilar competitor on the market and subject to "bona fide" marketing, a new CMS-created requirement not found anywhere in the statute. Even then, the price control is only lifted for the next selection cycle, not immediately. By that point the damage is done, with the artificially low government-imposed prices permanently altering the market and preventing generic and biosimilar manufacturers from realizing their investments. A narrow statutory path theoretically available for biosimilar manufacturers to ask CMS to delay the selection of biological products for the Program is too limited, opaque, and unreliable to mitigate the negative impact on biosimilar development.

The sweeping impact of the IRA on the market gives lie to the Government's attempt to rationalize the Program's constitutional defects by equating CMS with an ordinary market participant and relying on the fiction that participation in the price-control program is voluntary. The district courts' decisions upholding the IRA against the Appellants' constitutional challenges rely heavily on that fiction. Their judgments should be reversed.

ARGUMENT

I. The generic and biosimilar industries offer important benefits to the United States' healthcare system.

The generic and biosimilar industries have saved the U.S. healthcare system trillions of dollars, while diversifying the supply sources providing critical medicines to patients. But even with abbreviated approval pathways, the development of generic and biosimilar products requires significant investments. Government mandates that distort the market and upend existing economic incentives thus threaten to undermine competition.

A. Generics and biosimilars bring down costs while diversifying supply.

Four decades ago, Congress passed the Drug Price Competition and Patent Term Restoration Act (commonly known as the Hatch-Waxman Act), creating today's generics industry. The Hatch-Waxman Act shortens the pathway for FDA approval of generic drugs by permitting generic manufacturers to file an application "specifying that the generic has the 'same active ingredient as,' and is 'biologically equivalent' to, the already-approved brand-name drug." *FTC v. Actavis, Inc.*, 570 U.S. 136, 142 (2013) (citation omitted). By "allowing the generic to piggy-back on the pioneer's approval efforts," the Hatch-Waxman Act "speed[s] the introduction of low-cost generic drugs to market." *Id.* (citation omitted).

This abbreviated pathway to approval quickly transformed the healthcare market. By "making generic entry easier and less costly, the Hatch-Waxman Act helped increase the number of generic manufacturers producing the same drug," which in turn led the "average prescription price of a generic drug [to] fall[]." Cong. Budget Off., *How Increased Competition From Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* xiii (July 1998), https://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/6xx/doc655/pharm.pdf. Over the past decade, generic drugs have saved patients and the healthcare system almost $3 trillion. Ass'n for Accessible Meds., *Hatch-Waxman Turns 40* at 3 (Feb. 2024), https://accessiblemeds.org/sites/default/files/2024-02/AAM-Hatch-Waxman-White-Paper.pdf ("*Hatch-Waxman Turns 40*"). In 2022 alone, generics led to savings of almost $400 billion. *See* Ass'n for Accessible Meds., *The U.S. Generic & Biosimilar Medicines Savings Report* 8 (Sept. 2023), https://accessiblemeds.org/sites/default/files/2023-09/AAM-2023-Generic-Biosimilar-Medicines-Savings-Report-web.pdf ("*Savings Report*").

After the Hatch-Waxman Act revolutionized healthcare with respect to small-molecule drugs, Congress sought to replicate that success for biologics. Unlike "traditional [small-molecule] drugs, which are typically synthesized from chemicals," a "biologic is a type of drug derived from natural, biological sources such as animals or microorganisms." *See Sandoz Inc. v. Amgen Inc.*, 582 U.S. 1, 6

(2017). These biologics "often represent the cutting-edge of biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have no other treatments available." FDA, *What Are "Biologics" Questions and Answers* (Feb. 6, 2018), https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers ("*Biologics Questions and Answers*").

Recognizing the need to encourage competition among biologics, in 2010, Congress enacted the Biologics Price Competition and Innovation Act (BPCIA), which introduced an abbreviated pathway for the approval of "biosimilar" versions of existing innovator biologic drugs, 42 U.S.C. § 262. The BPCIA provides for a shortened FDA review and approval of a biologic product that is shown to be "highly similar" to, and to have "no clinically meaningful differences" from, an existing FDA-approved biologic product. *See id.* § 262(i)(2), (k). On the flip side, to foster innovation of new drugs, the BPCIA granted new biologics twelve years of regulatory exclusivity, during which time FDA cannot license any biosimilar versions that might otherwise compete with the innovator product in the market. *Id.* § 262(k)(7).

As the biosimilar industry continues to grow, biosimilars, like generics, offer significant costs-savings through "robust biosimilar price competition that creates not only lower prices on biosimilars, but also lower prices on brand biologics."

Savings Report, *supra*, at 9. This competition has contributed to "biosimilar average sales prices today [being] more than 50 percent lower than the brand biologic price at the time of biosimilar launch." *Id.* Biosimilars saved patients and the U.S. healthcare system $9.4 billion in 2022 alone and nearly $24 billion in total since the first biosimilar entry in 2015. *Id.* at 7.

In addition to this financial relief, biosimilars and generics also offer a more diverse supply of drugs. Without biosimilar or generic manufacturers, the brand-name drug manufacturer would be the only source of a given drug, and supplies of that drug would accordingly be susceptible to shortages if, for instance, the sole manufacturer encountered "manufacturing and quality problems, delays, [or] discontinuations." FDA, *Drug Shortages* (June 27, 2024), www.fda.gov/drugs/drug-safety-and-availability/drug-shortages; *see also* FDA, *Drug Shortages: Root Causes and Potential Solutions* at 6 (updated Feb. 21, 2020), https://www.fda.gov/media/131130/download?attachment (noting that drug shortages can occur in part because new manufacturers wanting to sell drugs to address shortages must obtain FDA approval). For instance, BCG Live—which is used to treat bladder cancer and marketed by a single company—has suffered from ongoing shortages since January 2019, forcing the manufacturer to "allocat[e] the drug to distributors based on past use," patients to "scour[] chat rooms looking for help," and "[m]edical groups [to] develop[] guidelines for using the reduced supply" and "giv[e] top priority to new

patients."[2] But with the entry of biosimilars and generics, the number of sources for a medicine increases, reducing the risk of shortages and helping to ensure that patients receive the medication they need. *See* FDA, *Generic Drugs Can Help Promote Health Equity*, www.fda.gov/media/173765/download ("Generic drugs can help stabilize the supply of medicines and reduce the risk of drug shortages.").

B. The development of generics and biosimilars requires substantial investments and therefore depends on market incentives to succeed.

The benefits realized from generic and biosimilar competition depend on manufacturers' willingness to invest substantial amounts of time and money to bring these products to market. For example, Teva in just one year (2020) "invested nearly $1 billion in R&D activities and had more than 1,160 generic products in its development pipeline." Teva, *Generic Medicines and R&D* (Nov. 11, 2021), www.tevapharm.com/news-and-media/feature-stories/generics-medicine-development/.

Investment is particularly intensive for the development of biosimilars, because "most biologics are complex mixtures that are not easily identified or

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[2] Laurie McGinley, Wash. Post, *Low Prices of Some Lifesaving Drugs Make Them Impossible to Get* (June 18, 2019), https://www.washingtonpost.com/national/health-science/low-prices-of-some-lifesaving-drugs-make-them-impossible-to-get/2019/06/18/abd03190-66bb-11e9-82ba-fcfeff232e8f_story.html; FDA, *CBER-Regulated Products: Current Shortages* (June 20, 2024), https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-regulated-products-current-shortages (listing BCG Live as ongoing shortage); Merck, *Facing Global Shortage, Merck Commits to Meeting Patient Demand* (Jan. 24, 2024), https://www.merck.com/stories/facing-a-global-shortage-merck-commits-to-meeting-patient-demand/.

characterized," which makes research and development especially time- and capital-intensive. *Biologics Questions and Answers*, *supra*; *see also* FDA, *Review and Approval* (Dec. 13, 2022), www.fda.gov/drugs/biosimilars/review-and-approval. Moreover, even under the BPCIA's abbreviated pathway, "biosimilar drugs must still be put through some clinical trials," adding to development expenses. Cong. Budget Off., *Research and Development in the Pharmaceutical Industry* 22 (Apr. 2021), www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf. As a result, a typical biosimilar costs $100 million to $300 million to develop and takes six to nine years to go from analytical characterization to approval" with "the probability of success remain[ing] low." Miriam Fontanillo, *et al.*, McKinsey & Co., *Three Imperatives for R&D in Biosimilars* (Aug. 19, 2022), https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars.

The investments required to market a successful biosimilar continue even after securing FDA approval. Patent holders often bring lengthy and costly infringement lawsuits challenging a biosimilar launch. *See, e.g.*, *Sandoz*, 582 U.S. at 7-11 (describing BPCIA's framework for infringement litigation). And once a biosimilar does launch, the manufacturer typically must engage in significant marketing efforts since only a relatively small subset of biosimilars—those deemed "interchangeable," 42 U.S.C. § 262(k)(4)—are able to utilize automatic substitution

laws. *See* Sophia Humphreys, Am. J. of Managed Care, *Understanding Interchangeable Biosimilars at the Federal and State Levels* (Aug. 16, 2023).

Thus, although biosimilars have already produced significant gains for patients and the healthcare system, the industry is still young and its continued development is fragile given the scale of the investments required. The BPCIA operates within the context of an existing market structure; for the law's incentives to work, biosimilar manufacturers must be able to set prices consistent with market opportunity and to make plans based on expected market prices and competition several years down the line.

Generics and biosimilar manufacturers can invest in developing products only if they can reliably expect a return on that investment. *See* Dana Goldman *et al.*, *Mitigating the Inflation Reduction Act's Adverse Impacts on the Prescription Drug Market* 5 (Apr. 2023) (explaining that "generic drugs require a sufficiently discounted price … to attract a large portion of market share away from the branded market," and that generic manufacturers may not enter if they face lower revenues). The appeal of the abbreviated approval pathways comes from the difference between brand prices and the prices at which generic and biosimilar manufacturers can both draw market share away from the brand and still recoup development and marketing costs. Threats to this model undermine the premises on which successful generic and biosimilar competition is based.

II. The IRA, as implemented by CMS, will stifle generic and biosimilar competition through market-distorting coercion.

The IRA steamrolls the market incentives on which the BPCIA relies. Under the IRA, the federal government (CMS)—historically prohibited from "interfering" in private price negotiations between drug manufacturers, pharmacies, and insurance plan sponsors, *see* 42 U.S.C. § 1395w-111(i) (2003)—can now take over pricing for high-Medicare-spend drugs before the congressionally enacted pathways for biosimilars or generics permit them to enter the market *and* even when biosimilar or generic competition already exists. The limited mechanisms available in the IRA to protect generic and biosimilar competition are facially inadequate; indeed, the uncertainty they foster only exacerbates the market disruption and disincentivizes developers of lower-cost generic and biosimilar drugs.

A. Government-imposed prices for selected brand drugs will directly impact the market for corresponding generic and brand medicines.

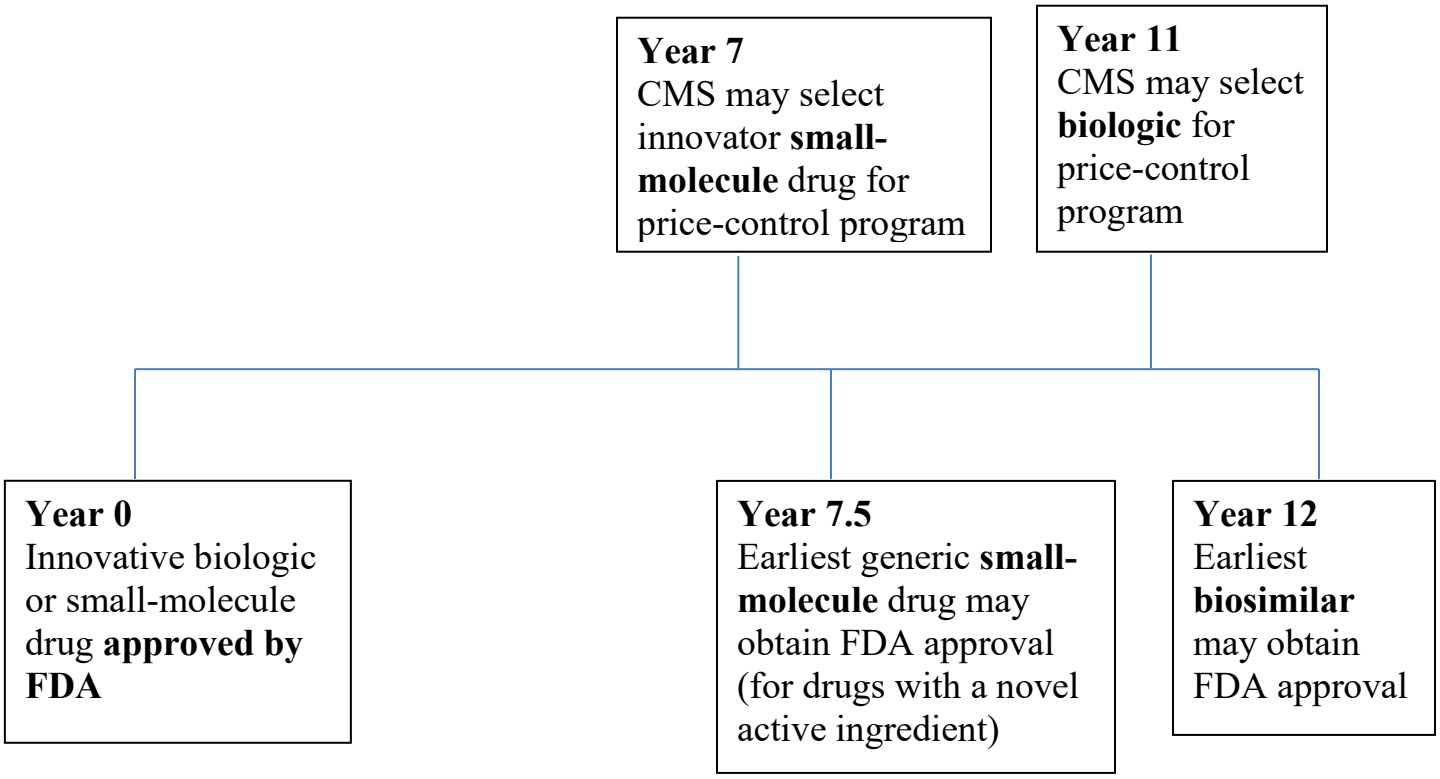
As described in Appellants' briefs, the IRA directs the Secretary of HHS to establish the Program wherein CMS selects top-spend drugs under Medicare to be subject to "price negotiations." 42 U.S.C § 1320f-1(a). CMS may select small-molecule drugs for price negotiations if there is no approved and "marketed" generic version of the drug and seven or more years have elapsed since FDA's initial approval of the first indication for the drug. *Id.* § 1320f-l(e)(l)(A). CMS may select

a biologic drug if there is no licensed and "marketed" biosimilar and at least eleven years have elapsed since the date of its licensure. *Id.* § 1320f-l(e)(l)(B).

These timing windows for selection have significant negative implications for the development of generics and biosimilars. Although the IRA formally excludes products that already face generic and biosimilar competition from the Program, the statute creates a race between CMS and follow-on competitors that the generic and biosimilar industries will almost invariably lose. As noted, p. 12, *supra*, and in the graphic below, p. 14, *infra*, newly licensed biologics are entitled to 12 years of regulatory exclusivity, during which FDA cannot approve corresponding biosimilar products. 42 U.S.C. § 262(k)(7). And even after that time, biosimilars typically face patent suits that often slow down market entry. Because the IRA authorizes CMS to select a biologic for the price-control program after 11 years, biosimilar manufacturers have no chance to get onto the market before the highest-value biological products are selected. Generic drugs face the same situation. Whereas CMS can select a high-value drug for the Program after 7 years, FDA generally cannot approve a generic version of a drug with a novel active ingredient for at least 7.5 years after the brand was approved (and often longer). *See* 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii).[3]

[3] FDA cannot even accept the filing of a generic application for review until four years after the approval of the new-chemical entity, and even then only if the generic manufacturer certifies that its product does not infringe a valid patent, which is

The graphic below illustrates the timing problem for generic and biosimilar manufacturers:



Thus, the IRA stacks the deck against genuine competition from generic and biosimilar manufacturers. The Government bars these companies from entering the market during a period of government-conferred exclusivity to brand manufacturers. During this period, manufacturers of the innovative treatment do not have to compete with others and can set their prices high enough to recoup their research and development costs. But the IRA permits CMS to select biologic and small-

typically a prelude to patent litigation and an automatic stay. 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii).

molecule drugs for participation in the Program before their exclusivity periods expire, meaning that by the time biosimilars and generics can enter the market, the Government has already imposed artificially low prices. Biosimilar and generic manufacturers thus never have the chance to compete in an open market. The Government rewrites the rules of the marketplace to secure its own advantage, restricting market access and then imposing price mandates via illusory "negotiations" that undercut the market opportunity for new entrants.

The distorting effect of the IRA on the marketplace will be significant. As Appellants describe, during the putative "price negotiations," CMS sets a "Maximum Fair Price" for the selected drug. 42 U.S.C. § 1320f-2(a)(l). The selected drug must be made available to Medicare beneficiaries at the government-mandated price beginning the first day of the first "price applicability year" for the selected drug, which falls roughly two years after the selection date. *Id.* There is no serious question that CMS's price will be far below market value; that is, after all, the point of the IRA regime. The statute thus requires CMS to set the price of a selected biologic drug (or any small-molecule brand-name drug approved for 12-16 years without competition) at no higher than 65% of the average price paid by non-governmental purchasers, and at no higher than 40% of the average price paid by non-governmental purchasers for selected drugs that have been approved for longer than 16 years by the time the mandated price takes effect. *Id.* § 1320f-3(c).

Generic and biosimilar manufacturers do not participate directly in the Program, but the government-mandated prices for the corresponding brand product will effectively bind them too while the brand product remains selected. Generic and biosimilar manufacturers will have no ability to charge market-based prices while the corresponding brand product is forced to sell at the government-mandated price. On average, biosimilars have launched at prices averaging a discount of 50% compared to the corresponding brand biologic price at the time of biosimilar launch. *Savings Report*, *supra*, at 26. When CMS orders the brand to charge prices at that level or lower, there is no practical room for biosimilars to compete. As a result, the Program threatens to "erode the value proposition for a potential biosimilar [or generic] entrant"; once CMS mandates "a significantly lower price for a given product, biosimilars [or generics] in the pipeline may then carry a lower value proposition than initially expected, while others may exit the market or never launch." Mark Von Eisenburg, Avalere, *How Will the IRA Impact the Future of Biosimilars?* (Aug. 17, 2023), https://avalere.com/insights/how-will-the-ira-impact-the-future-of-biosimilars; *see also* Goldman, *supra*, at 5 ("[T]he decrease in brand prices due to negotiations could reduce the prices that any generic firm can charge, disincentivizing generics from … entering the market.").

In fact, the IRA not only undermines the market for biosimilar entrants by pushing down prices, but it also compromises their ability to compete with a selected

brand product. Beginning January 1, 2025, a new Medicare Part D discount program will replace the previous program. *See* Inflation Reduction Act of 2022, Pub. L. 117-169, § 11201 (codified as §§ 1860D-14C, 1860D-43 of the Social Security Act (42 U.S.C. § 1395w-114c; 42 U.S.C. § 1395w-153)). Under it, every manufacturer that seeks Medicare Part D coverage for certain "applicable drugs"—including both brand-name biologics and biosimilars dispensed to Medicare enrollees—must agree to a 10%-20% discount (depending on circumstances). The IRA exempts drugs selected for the Program (and subject to the government-price mandate) from this additional discount obligation. *See* 42 U.S.C. § 1395w-114c(g)(2). Because biosimilars are not formally selected, they are disadvantaged twice over: the government-mandate price for the brand drives down what biosimilar manufacturers can plausibly charge, but they also remain subject to the additional discount. The inevitable result will be to discourage biosimilar competition, which will harm patients who lose access to alternative supplies of critical medicines.

B. The IRA fails to protect biosimilars from the market disruption caused by the Program and government-coerced price erosion.

In seeming recognition of the threat posed by the IRA's pricing mandates for the viability of biosimilars, the statute includes certain limited concessions for potential biosimilar competition. But the exemptions provided are facially inadequate, and serve only to underscore the market disruption caused by the IRA.

1. As implemented by CMS, the IRA lifts its price mandates only after the generic or biosimilar market is already decimated.

Under the IRA, only "single source drugs"—*i.e.*, those that do not face generic or biosimilar competition—are "negotiation-eligible." 42 U.S.C. § 1320f-1(d), (e)(1). But CMS nonetheless enforces its price mandates even in the face of date-certain generic or biosimilar market entry.[4]

A drug is ineligible for selection if a generic is "approved and marketed" or a biologic is "licensed and marketed." *Id.* § 1320f-1(e)(1)(A)-(B). Although the "interpretation of the meaning of statutes … [is] exclusively a judicial function," *Loper Bright Enters. v. Raimondo*, 144 S. Ct. 2244, 2258 (2024) (citation omitted), CMS has grafted a "bona fide marketing" requirement onto the statute's standard, under which the agency will only de-select a drug if CMS determines there is a biosimilar or generic version that provides "meaningful competition" to the selected drug based on a vague "holistic" review standard. *See* CMS, *Medicare Drug Price Negotiation Program: Revised Guidance* 72-75 (June 30, 2023), https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf ("*Program Guidance*"). Moreover, according to CMS, the first year a

[4] Indeed, as explained in Section II.C, *infra*, STELARA, a biologic drug, was selected for the Program, even though several manufacturers had already submitted biosimilar applications and two manufacturers had publicly announced settlements with specific biosimilar entry dates. As a result, CMS has determined price mandates will apply notwithstanding robust biosimilar competition beginning even before the 2026 effective date.

drug can be de-selected from the Program is the year that begins at least nine months after CMS determines that a biosimilar or generic version of the drug is approved and "bona fide market[ed]." *Id.*; *see* 42 U.S.C. § 1320f-l(c)(l).

Putting this together, CMS will require a selected drug manufacturer to remain in the Program and comply with the government-mandated price unless CMS determines *before or during the negotiation period* that a biosimilar or generic is both approved and "bona fide marketed." *Program Guidance*, *supra*, at 71. If a generic or biosimilar launch occurs *after* the negotiation period, then CMS understands the IRA to "require[] a selected drug that is included on the selected drug list to remain a selected drug for that year and each subsequent year" until the year that begins at least nine months after the date on which CMS determines the bona fide marketing requirement is met. *Id.*

CMS's extra-statutory "bona fide marketing" requirement not only introduces uncertainty but also makes it extremely unlikely that a biosimilar or generic will be able to save its market from government induced price erosion. The period between selection of a drug and the end of negotiations is only 9 months (11 months for the first year). *See* 42 U.S.C. § 1320f(b). CMS requires biosimilars or generics to prove "bona fide marketing" before the end of that 9-month period. For biosimilar manufacturers targeting biologics selected for IRA negotiations 11-12 years after initial approval, beating the negotiation deadline is impossible. *See* pp. 13-15, *supra*.

If a biosimilar or generic cannot obtain approval and engage in sufficient marketing to satisfy CMS's "holistic" inquiry before the negotiation deadline for a selected drug, the government-mandated price will go into effect even if biosimilars or generics have been on the market for over a year. Rather than allowing biosimilars and generics to set market-competitive prices, the IRA pulls the rug out from under those manufacturers, distorting the market with coercively set, artificially lower prices. Even if CMS de-selects the reference drug in a later year, the damage will have been done: the government-mandated price will have set market expectations, depriving biosimilars and generics of the market conditions on which their development was premised. *See, e.g.*, *Polymer Techs., Inc. v. Bridwell*, 103 F.3d 970, 976 (Fed. Cir. 1996) ("[r]equiring purchasers to pay higher prices after years of paying lower prices … is not a reliable business option").

CMS's implementation of the statute creates a deeply illogical gap: if a generic or biosimilar launches (and satisfies CMS's vague "bona fide marketing" standard) during the negotiation period, CMS will exclude the product from the Program. *Id.* But if biosimilar or generic competition commences outside that window—but *before* price mandates go into effect—CMS imposes the price mandates anyway, only lifting them much later after the damage to the market is done. *Id.*

2. The biosimilar "delay" provision is too limited and opaque to meaningfully protect biosimilar competition.

The IRA nominally acknowledges that biologics should not be selected into the Program if biosimilar competition is imminent. Section 11002 provides a "[s]pecial rule to delay selection and negotiation of biologics for biosimilar market entry" (the "biosimilar-delay provision"). 42 U.S.C. § 1320f-1(f). Under that rule, a biosimilar manufacturer can request that CMS delay the selection of a brand-name biologic into the Program if the biologic will have been licensed for fewer than 16 years by the time the government-mandated price would take effect, based on a "high likelihood" that the biosimilar will be licensed and marketed by the time the price mandate would go into effect if the branded biologic were selected. *See Program Guidance*, *supra*, at 109-112. This requires compiling and submitting substantial documentation to show CMS that (1) the reference drug's patents are unlikely to prevent the biosimilar from being marketed and (2) the biosimilar will be operationally ready to market within two years of when the reference product would otherwise be selected into the Program. 42 U.S.C. § 1320f-1(f)(1)(B)(ii).

In practice, however, the relief supposedly afforded by the biosimilar-delay provision is highly unreliable and imposes additional costs on biosimilar manufacturers. Biosimilar manufacturers can only guess as to what drugs CMS might select in any given program year. But biosimilar manufacturers must submit any delay request to CMS before the reference biologic is selected, forcing

biosimilar manufacturers to bear the burdens of preparing and submitting a delay request merely to hedge against the possibility that the reference product will be selected. *Id.* § 1320f-1(f)(1)(B)(i)(I). Moreover, if there are relevant developments that postdate initial selection—for example, a patent settlement and licensed entry date that allows a biosimilar to enter the market after negotiation but before price mandates become effective—the biosimilar manufacturer is simply out of luck. *See* pp. 12-15, *supra*.

The biosimilar-delay provision also provides no meaningful recourse for biosimilar manufacturers if CMS rejects their request. Delay requests are not public, and CMS conducts its review behind closed doors. CMS notifies the requestor if a delay has been granted or denied only after it announces what drugs it has selected for the Program. CMS is not required to provide any explanation or justification for its determination, and there is no judicial review available for its determinations. *See Program Guidance*, *supra*, at 113.

In sum, the biosimilar-delay provision provides no meaningful assurance that CMS, whose review is shrouded in secrecy, will respect the expectation interests of manufacturers who have invested years of research and development into bringing a biosimilar to market. Without that kind of assurance, biosimilar manufacturers deciding whether to start or continue investing millions of dollars into bringing a lower-cost alternative to market undertake substantial risk in assuming that the

market will not be flattened by the IRA by the time the biosimilar can reach the market several years later.

C. The example of selected product STELARA shows how the IRA will distort the market.

The market distortions and harms to biosimilars described above are already happening. One of the drugs selected in the first round of IRA negotiations—Janssen's biologic drug STELARA (ustekinumab)—provides a case study.

STELARA is a monoclonal antibody indicated for the treatment of several autoimmune disorders including Crohn's disease and ulcerative colitis. STELARA was approved on September 25, 2009, and was selected into the IRA Negotiation Program on August 29, 2023. At the time CMS selected STELARA, several manufacturers had already submitted applications for biosimilar versions of STELARA to FDA, and two had publicly announced settlements with date-certain biosimilar entry dates. One, Amgen, had announced (in May 2023) that it had settled patent litigation with Janssen on terms that would allow it to start selling its biosimilar no later than January 1, 2025.[5] And on June 12, 2023, Teva and Alvotech announced they had settled with Janssen on terms that would allow for the launch of

[5] Blake Brittain, Reuters, *Amgen Settles Patent Lawsuit Over Biosimilar of J&J's Big-Selling Stelara* (May 23, 2023), https://www.reuters.com/business/healthcare-pharmaceuticals/amgen-settles-jj-patent-lawsuit-over-drug-similar-blockbuster-stelara-2023-05-23/.

a biosimilar product no later than February 21, 2025.[6] FDA approved Amgen's biosimilar version of STELARA on October 31, 2023, roughly two months after CMS selected STELARA for price negotiations.[7] Since then, as of the date of this filing, two more biosimilar versions of STELARA have been approved by FDA: Teva and Alvotech's SELARSDI (approved April 16, 2024), and Sandoz and Samsung Bioepis's PYZCHIVA (approved July 1, 2024).

As reflected in public statements from the companies, the licensed biosimilar versions of STELARA should launch by January-February 2025—roughly a year before the government-mandated price reductions for STELARA could go into effect.[8] Although biosimilar competition was imminent when CMS selected STELARA, there was no way for biosimilar manufacturers to request that CMS delay the selection to allow for biosimilar competition. At the time CMS selected

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[6] Alvotech, *Alvotech and Teva Secure U.S. License Date for AVT04, a Proposed Biosimilar to Stelara* (June 12, 2023), https://investors.alvotech.com/news-releases/news-release-details/alvotech-and-teva-secure-us-license-date-avt04-proposed.

[7] FDA, *FDA Approves Interchangeable Biosimilar for Multiple Inflammatory Diseases* (Oct. 31, 2023), www.fda.gov/news-events/press-announcements/fda-approves-interchangeable-biosimilar-multiple-inflammatory-diseases.

[8] Sandoz, *FDA Approves Biosimilar Pyzchiva (ustekinumab-ttwe), To Be Commercialized by Sandoz in US* (Jan. 7, 2024), https://www.sandoz.com/fda-approves-biosimilar-pyzchivar-ustekinumab-ttwe-be-commercialized-sandoz-us/; Teva, *Alvotech and Teva Announce U.S. FDA Approval of Selarsdi (ustekinumab-aekn), Biosimilar to Stelara (ustekinumab)* (Apr. 16, 2024), https://ir.tevapharm.com/news-and-events/press-releases/press-release-details/2024/Alvotech-and-Teva-Announce-U.S.-FDA-Approval-of-SELARSDI-ustekinumab-aekn-biosimilar-to-Stelara-ustekinumab/default.aspx.

STELARA for negotiations in August 2023, STELARA had been approved for fewer than 14 years. But by the time the government-mandated price becomes effective, it will have been approved for more than 16 years, thus eliminating any recourse to the biosimilar-delay provision. *See* p. 21, *supra*. Moreover, in implementing the IRA, CMS required biosimilar manufacturers to show, by May 2023, "[c]lear and convincing evidence that the Biosimilar will be marketed before September 1, 2025." *Program Guidance*, *supra*, at 110-113. That requirement was entirely unrealistic, as patent-litigation and FDA approval issues that have since been resolved could not be predicted with certainty years in advance.

Perhaps most troubling, under CMS's remarkable reading of the IRA, the launch of multiple biosimilar versions of STELARA in early 2025 will provide no relief from government price mandates. STELARA will remain a "selected" drug for 2026 and 2027, and a "negotiated" price will be applied to STELARA beginning January 1, 2026—even with multiple biosimilars on the market. *See* pp. 12-15, *supra*. Companies like Teva that invested many millions of dollars to develop a STELARA biosimilar will be deprived of a meaningful opportunity to realize their investments, as announcement of the government-mandated price and its subsequent imposition will upend the market.

III. The market-distorting impact of the IRA belies the Government's attempt to equate itself with an ordinary market participant.

The significant market-distorting effects of the IRA make clear that the Government is not an ordinary market participant, and contradict the Government's repeated refrain that Program participation is voluntary and that the Government is merely offering a price on which it is willing to deal.[9] Drug manufacturers have no real choice over whether to participate in the Program, and its distorting effects extend beyond even the companies selected to participate in a putative "negotiation."

To ensure that manufacturers can neither economically nor in good conscience refuse to participate in Medicare and Medicaid, the IRA flexes the Government's dominant market share while simultaneously adding onerous requirements to ensure that manufacturers cannot avoid participating. More specifically, the IRA provides that manufacturers seeking to avoid participating in the Program must terminate their Medicare Part D and Medicaid rebate agreements for not just the selected drug but for *all* drugs—a tying requirement that no ordinary market participant, even one with a dominant share, could levy on manufacturers. *See* 26 U.S.C. § 5000D(c). Medicare is "the largest federal program after Social

[9] *See* Mem. of Law in Support of Defs.' Opp'n to Pls.' Mot. for Summ. J. & Cross-Mot. at 19-25, *Bristol Myers Squibb Co. v. Becerra*, Nos. 23-cv-3335, 23-cv-3818 (D.N.J. Oct. 16, 2023), Dkt. No. 38-1 ("Gov't Summ. J. Mem."); Mem. of Law in Support of Defs.' Opp'n to Pls.' Mot. for Summ. J. & Cross-Mot. at 45-47, *AstraZeneca Pharms. LP v. Becerra*, No. 1:23-cv-931 (D. Del. Nov. 2, 2023), Dkt. No. 22.

Security" and "spends about $700 billion annually to provide health insurance for nearly 60 million aged or disabled Americans, nearly one-fifth of the Nation's population." *Azar v. Allina Health Servs.*, 587 U.S. 566, 569 (2019). Medicaid likewise serves a substantial proportion of the American population with over 75 million individuals enrolled in the program. Medicaid.gov, *March 2024 Medicaid & CHIP Enrollment Data Highlights* (updated June 28, 2024), https://www.medicaid.gov/medicaid/program-information/medicaid-and-chip-enrollment-data/report-highlights/index.html. Consequently, "[t]hrough Medicare and Medicaid, [the Government] pays for almost half the annual nationwide spending on prescription drugs." *Sanofi*, 58 F.4th at 699.

By requiring manufacturers to stop selling medication to approximately half of the entire market to avoid price mandates, the Government leverages its enormous market power and regulatory authority to coerce compliance. Congress plainly designed the IRA, with its all-or-nothing structure, to put forward an "offer" drug manufacturers cannot refuse. Medicare and Medicaid serve highly vulnerable communities, including elderly individuals, individuals with disabilities, and the indigent, and it is implausible that Congress would contemplate any genuine risk that these populations would lose access to critical medicines.

The Government's alternative suggestion that companies could avoid the mandate by divesting their interest in a selected drug[10] only serves to underscore the fiction that the Government is operating like a market participant. No mere market participant could require, on the pain of substantial financial penalties, that a company divest its interest in its hard-won asset purely to avoid being subjected to significant financial penalties. Moreover, the theoretical buyer of the selected drug post-divestment would still be subject to the Program and would still be required to sell the selected drug at an artificially low, mandated price. *See Program Guidance*, *supra*, at 131-32. The collateral damage on the generic and biosimilar marketplace would therefore be unchanged, with the suppressed prices (compounded by mandatory rebates) undermining incentives for generic and biosimilar manufacturers to invest and develop alternative supplies of valuable medicines. *See* pp. 16-17, *supra*. All that divestment would achieve is swapping out the brand manufacturer's name.

Ordinary, voluntary transactions do not fundamentally reorder entire marketplaces and snuff out effective competition. The Government acts here as a regulator whose mandates appropriate private industry for its own use, with the perverse effect that a law ostensibly intended to lower drug prices will undermine

[10] *See* Gov't Summ. J. Mem. at 8, 14, 17.

the ability of generic and biosimilar manufacturers to drive down costs through competition while increasing patient access through a diversified drug supply. The Court should reject the Government's constitutional defenses premised on the fiction that coercive pricing mandates are akin to voluntary commercial terms.

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As this Court has recognized, the Government "uses [its] market power to get drug makers to subsidize healthcare." *Sanofi*, 58 F.4th at 699. The government goes even further here. Its mandate that manufacturers provide selected drugs at low prices or else face financial ruin risks distorting the healthcare market and depriving millions of people of the life-saving treatments they need. This Court should not sustain the Government's unprecedented market intrusion.

CONCLUSION

The Court should reverse the judgments below.

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Respectfully submitted.

s/ *Brian T. Burgess*

Brian T. Burgess
Matthew Wetzel
Rohiniyurie Tashima
GOODWIN PROCTER LLP
1900 N Street, NW
Washington, DC 20036
(202) 346-4000
bburgess@goodwinlaw.com

Counsel for Amicus Curiae

Alexandra Lu
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Natasha E. Daughtry
GOODWIN PROCTER LLP
601 South Figueroa Street, Suite 4100
Los Angeles, CA 90017
(213) 426-2500

CERTIFICATE OF SERVICE

I hereby certify that on July 19, 2024, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Third Circuit using the Court's CM/ECF system. Counsel for all parties to the case are registered CM/ECF users and will be served by the CM/ECF system.

s/ *Brian T. Burgess*
Brian T. Burgess

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Rule of Appellate Procedure 29(a)(5) because the brief contains 6,210 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(f).

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July 19, 2024

s/ *Brian T. Burgess*
Brian T. Burgess