



June 2025

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Cooley Rx

Life Sciences Litigation:  
Introduction to Biosimilars Litigation

# Agenda

1. Introduction
2. BPCIA Basics
3. Patent Dance
4. First Wave Litigation
5. Second Wave Litigation

# Biologics Price Competition and Innovation Act

- Enacted in March 2010
- Provides an abbreviated approval pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed “reference product”
- Key features:
  - Abbreviated pathway for approval of biosimilar/interchangeable products
  - Market exclusivities for reference products and interchangeable biosimilars
  - Framework for patent dispute resolution

# Biological Products/Reference Products

## (i) "BIOLOGICAL PRODUCT" DEFINED

In this section:

**(1)** The term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

**(4)** The term "reference product" means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).

# Biological Products | Proteins

(6) A protein is any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size. When two or more amino acid chains in an amino acid polymer are associated with each other in a manner that occurs in nature, the size of the amino acid polymer for purposes of this paragraph (h)(6) will be based on the total number of amino acids in those chains, and will not be limited to the number of amino acids in a contiguous sequence.

# Drug or Biological Product?

- There have been several challenges as to whether or not a therapy is a drug or a biologic
  - *Eli Lilly & Co. v. Becerra*, No. 1:24-cv-01503 (S.D. Ind.)
  - *Ipsen Biopharmaceuticals, Inc. v. Becerra*, 108 F.4th 836 (D.C. Cir. 2024)
  - *Teva Pharms. v. FDA*, 514 F. Supp. 3d 66 (D.D.C 2020)
- Why challenge?
  - Biologics generally not eligible for exemptions for compounded drugs under FDCA Sections 503A and 503B
  - Longer regulatory exclusivity as a biologic

# Exclusivities for Reference Products

- 4-year data exclusivity
  - Prevents FDA from accepting a biosimilar application
- 12-year marketing exclusivity
  - Prevents FDA from approving a biosimilar application
  - Starts on date reference product “first licensed”
- Data and marketing exclusivities only block a biosimilar application, not a full BLA
- Pediatric and Orphan Drug exclusivities both available

# No Additional Regulatory Exclusivity

- Supplemental BLAs
- A BLA filed by the same reference product sponsor or a licensor, predecessor in interest, or other related entity for:
  - A change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength, or
  - A structural modification that does not result in a change in safety, purity, or potency

# Biosimilars

**(2)** The term “biosimilar” or “biosimilarity”, in reference to a biological product that is the subject of an application under subsection (k), means—

**(A)** that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

**(B)** there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

# Biosimilar Requirements

- Showing of “biosimilarity” based on:
  - (1) analytical studies showing “highly similar” to reference product notwithstanding minor differences in inactive components,
  - (2) assessment of toxicity (typically animal studies), and
  - (3) clinical studies to demonstrate safety, purity and potency in one or more indications
- Biosimilar indication(s) previously approved for the reference product
- Same route of administration, dosage and strength as reference product

# Interchangeables

**(3)** The term “interchangeable” or “interchangeability”, in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

# Interchangeable Requirements

- Must be “biosimilar” to reference product
- Must also show that:
  - The biosimilar will produce **same clinical results** as reference product **in any given patient**; and
  - Any risk in terms of safety or diminished efficacy from switching between reference product and biosimilar is no greater than using the reference product without switching.
  - May need a switching study to support for this requirement

# Exclusivity for Interchangeables

- First interchangeable receives exclusivity
- Prevents FDA from **approving another interchangeable** that relies on the same reference product until the earlier of:
  - 1 year after first commercial marketing of first interchangeable;
  - 18 months after (i) a final court decision on all patents in suit or (ii) dismissal, of an action “instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product”;
  - 42 months after approval of first interchangeable “if the applicant that submitted such application has been sued under subsection (l)(6) and such litigation is still ongoing”;
  - 18 months after approval of first interchangeable “if the applicant that submitted such application has not been sued under subsection (l)(6)”

# The Purple Book

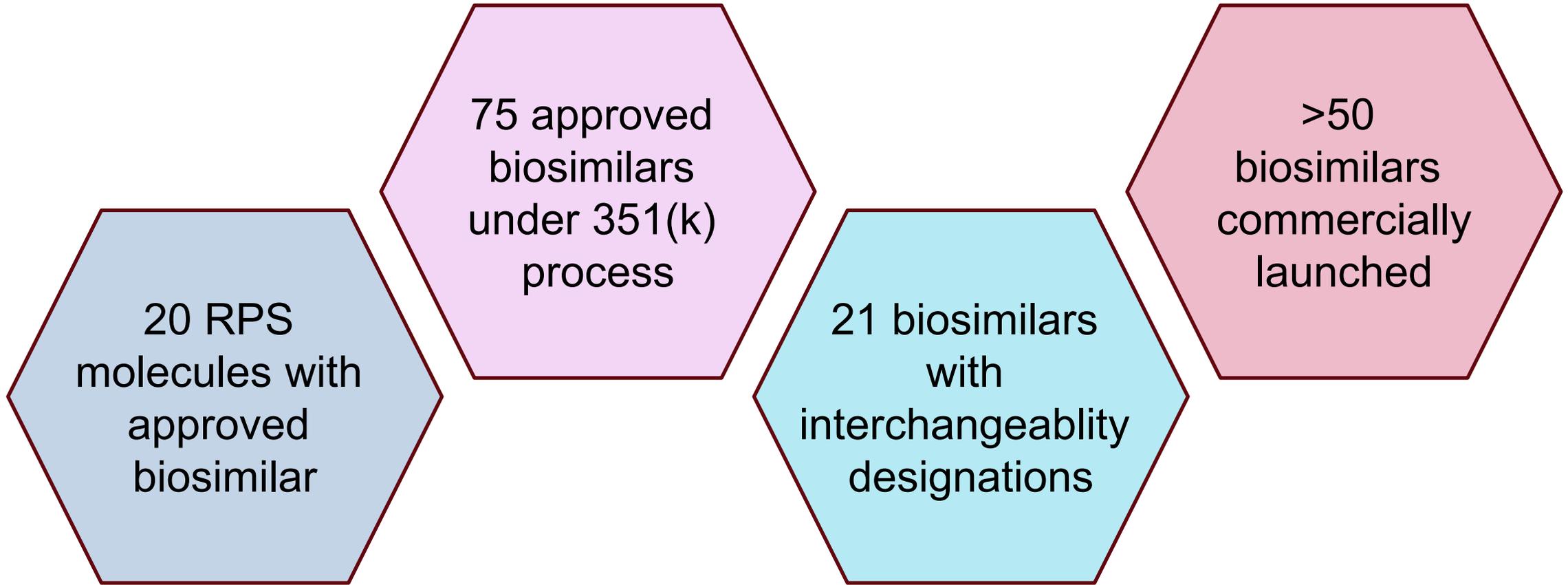
- Contains information on all FDA-approved biologics, including reference products, biosimilars, and interchangeable
- No requirement for sponsor to list patents when new product approved
- Sponsor required to provide any patent list given to a biosimilar in the patent dance within 30 days (see 42 U.S.C. § 262(k)(9)(A)(iii))



**Purple Book**  
**Database of Licensed Biological Products**



# BPCIA: A Success?



# BPCIA Patent Disputes

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# Overview

- Exchange of patent information (the “Patent Dance”)
  - Begins when biosimilar notifies the RPS that FDA has accepted a biosimilar BLA
  - Followed by an exchange of information between the parties to identify patent disputes
  - The process is designed to result in a list of patents for first wave litigation
- First wave litigation
  - The RPS can initiate the first wave of litigation based on the patent list that results from the dance
- Second wave litigation
  - Triggered by biosimilar's 180-day notice of intent to commercially market the product
  - During this second phase, the RPS can assert any patent identified during the patent dance that was not included in the first wave
  - If the RPS does not bring a preliminary injunction action or if the court refuses to grant one, the biosimilar can launch while litigation proceeds

# Patent Dance Steps

- Biosimilar files application
- **Step 1:** Biosimilar provides RPS with biosimilar application
- **Step 2:** RPS provides biosimilar with patent list
- **Step 3:** Biosimilar provides patent list and a detailed statement of invalidity, unenforceability, and non-infringement
- **Step 4:** RPS responds to detailed statement
- **Step 5:** Parties negotiate patents to be litigated
- **Step 6:** RPS files complaint of patent infringement

# Step 1: Biosimilar Provides Biosimilar BLA

§ 262(l)(2)

- The biosimilar applicant “shall provide” its biosimilar application (351(k) BLA), including information regarding its manufacturing process, to the RPS within 20 days of FDA’s notice that its application is under review
- Confidential access given to RPS’s attorneys, subject to a protective order, and may be given to a “representative” of a patent owner if patent is licensed by the RPS
- Confidential access to the full application is contemplated

# Patent Dance Not Mandatory

- Courts cannot force biosimilars to comply with the first step of the patent dance. *Amgen v. Sandoz*, 582 U.S. 1 (2017).
  - Despite its command that an applicant “shall provide” its application and manufacturing information, the statute also “provides a remedy for an applicant’s failure to turn over its application and manufacturing information”
- If the biosimilar does not comply with § 262(l)(2), the sponsor can file a declaratory judgment action on “any patent that claims the biological product or use of the biological product.” 42 U.S.C. § 262(l)(9)(C)

# Step 2: RPS Provides Patent List

§ 262(l)(3)(A)

- Within 60 days of being provided the application, RPS is required to provide biosimilar with:
  - a list of patents that could reasonably be asserted
  - a list of patents that RPS is willing to license to biosimilar
- RPS must supplement its list with relevant newly issued or licensed patents within 30 days of issuance or licensing.
  - Any newly issued or licensed patents listed on the RPS supplement will be subject to the second wave of patent litigation.

# 35 U.S.C. § 271(e)(6)(C)

**(C)** The owner of a patent that should have been included in the list described in section 351(l)(3)(A) of the Public Health Service Act, including as provided under section 351(l)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.

# Step 3: Biosimilar Provides Patent List and Detailed Statement

§ 262(l)(3)(B)

- Within 60 days of receiving RPS's patent list, biosimilar:
  - May provide a list of patents that biosimilar believes could reasonably be asserted by the RPS
  - Must provide the RPS with:
    - a detailed statement setting forth the factual and legal basis why each patent listed by the RPS or the biosimilar is invalid, unenforceable or will not be infringed
    - OR
    - a statement that biosimilar does not intend to begin marketing its product before such patent expires.
  - Must provide RPS with a "response" regarding each patent RPS designates for licensing

# Step 4: RPS Provides Detailed Statement

§ 262(l)(3)(C)

- Within 60 days receiving the biosimilar's patent list and detailed statement, the RPS must provide a detailed statement in response to the biosimilar's detailed statement
- Must explain, on a claim-by-claim basis, why each patent included in the biosimilar's detailed statement is infringed, valid, and enforceable

# Step 5a: Mandatory Negotiation of Patents

§ 262(l)(4) and § 262(l)(6)(A)

- For 15 days after receiving the RPS's responsive detailed statement, the parties must engage in good faith negotiations to agree on a list of patents for the first wave litigation
- If the parties agree on a list of patents within the 15 days, the RPS must bring an infringement action within 30 days for each agreed-upon patent.
  - The biosimilar must notify the FDA of the complaint of infringement within 30 days.
  - The FDA will subsequently publish a notice of the complaint in the Federal Register.

# Step 5b: No Agreement

§ 262(l)(5)

- If the parties cannot reach an agreement within 15 days, an additional set of patent exchange procedures must be followed:
  - Biosimilar will tell RPS the number of patents it believes should be subject to first wave litigation
  - Within 5 days of receiving that number, the parties must simultaneously exchange lists of patents that they believe should be litigated
    - The number of patents listed by the RPS cannot exceed the number identified by the biosimilar
    - If the biosimilar lists zero patents than the RPS may list one patent
  - RPS must file a complaint for infringement within 30 days for each patent identified in both the biosimilar and RPS's lists

# Step 6: PRS Files Suit

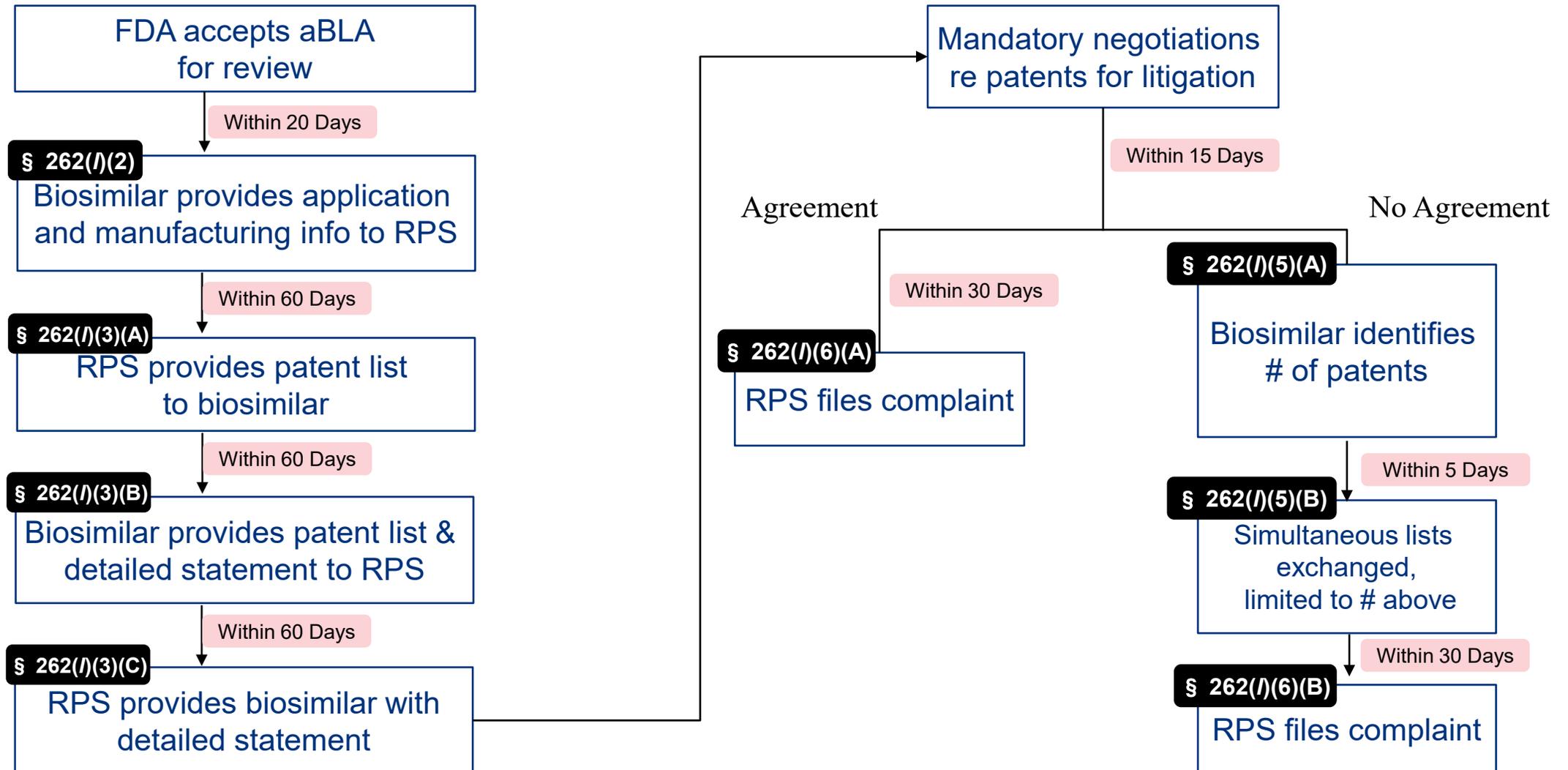
§ 262(l)(6)(B)

- RPS must file a complaint for declaratory judgment of infringement 30 days after:
  - If agreement is reached, the date the parties reach agreement on a list of patents to be litigated, or
  - If the parties do not reach agreement, the date of simultaneous exchange of patent lists
- Jurisdiction: the RPS has jurisdiction to file a declaratory judgment action because the 35 U.S.C. § 271(e)(2)(C) makes the filing of a biosimilar application an artificial act of patent infringement

# Limitation to Reasonable Royalty

**(B)** In an action for infringement of a patent described in subparagraph (A), the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty.

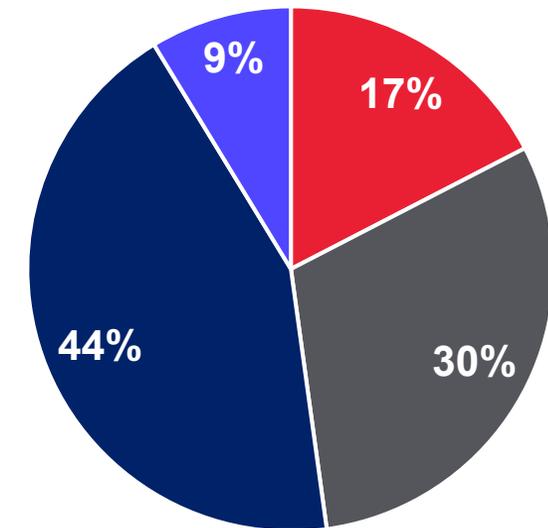
# The Patent Dance



# Dance Statistics

- Since the BPCIA's inception, parties have completed a full patent dance in greater than half of the disputes
- Recently, parties have engaged completed the dance less frequently

Trends over past 5 years (since 2019):



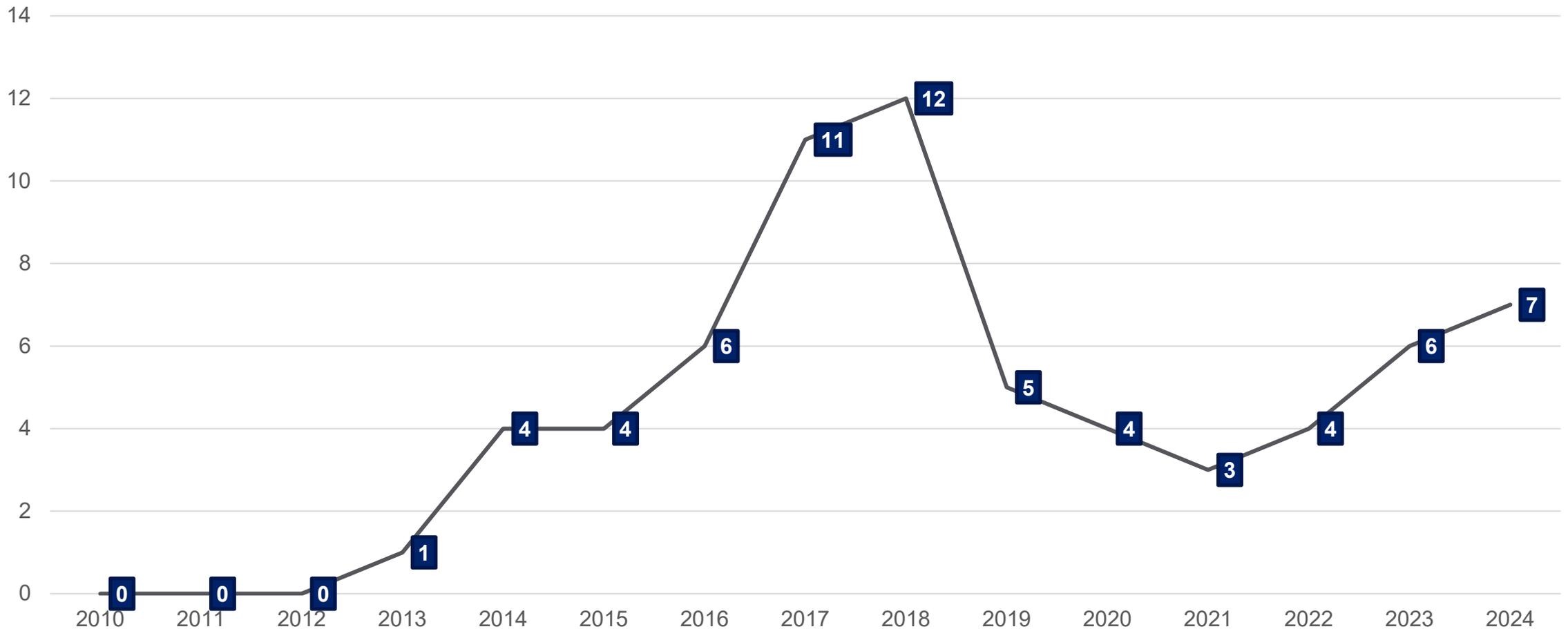
■ No dance ■ Partial Dance ■ Full Dance ■ Unknown

# Second Wave Litigation

§ 262(l)(8)(A)

- Notice of Commercial Marketing ( § 262(l)(8)(A))
  - Biosimilar must provide notice to RPS of intent to commercially market biosimilar not later than 180 days before first commercial marketing
  - Notice of Commercial Marketing required whether or not the parties engaged in patent dance, *Apotex Inc. v. Amgen Inc.*, 827 F.3d 1052 (Fed. Cir. 2016)
  - Biosimilar “may provide notice either before or after receiving FDA approval” (*Sandoz v. Amgen Inc.*, 137 S. Ct. 1664, 1668 (2017)).
- Preliminary injunction ( § 262(l)(8)(B))
  - After 180-day notice, but **before** the date of such commercial marketing, RPS may seek a preliminary injunction based on any patent that was originally identified in either party’s patent list during the dance but not included on any agreed upon or simultaneously exchanged patent list ( § 262(l)(8)(B))
  - Preliminary injunction may seek to prevent biosimilar from engaging in manufacture or sale prior to litigation resolution

# BPCIA Cases Filed by Year



# Current Ongoing BPCIA Litigation

## Ongoing Cases pertain to:

- Tysabri® (natalizumab)
  - One case against biosimilar Sandoz
- Eylea® (aflibercept)
  - Five cases (MDL) against biosimilars Celltrion, Samsung Bioepis, Formycon, Amgen, and Sandoz
- Xgeva®/Prolia® (denosumab)
  - Two remaining cases against biosimilars Samsung Bioepis and Accord

## Resolved Litigation regarding 12 RPS products:

- Actemra® (tocilizumab)
- Avastin® (bevacizumab)
- Enbrel® (etanercept)
- Epogen®/Procrit® (epoetin alfa)
- Herceptin® (trastuzumab)
- Humira® (adalimumab)
- Neulasta® (pegfilgrastim)
- Neupogen® (filgrastim)
- Remicade® (infliximab)
- Rituxan® (rituximab)
- Soliris® (exulizumab)
- Stelara® (Ustekinumab)

# The Next Wave

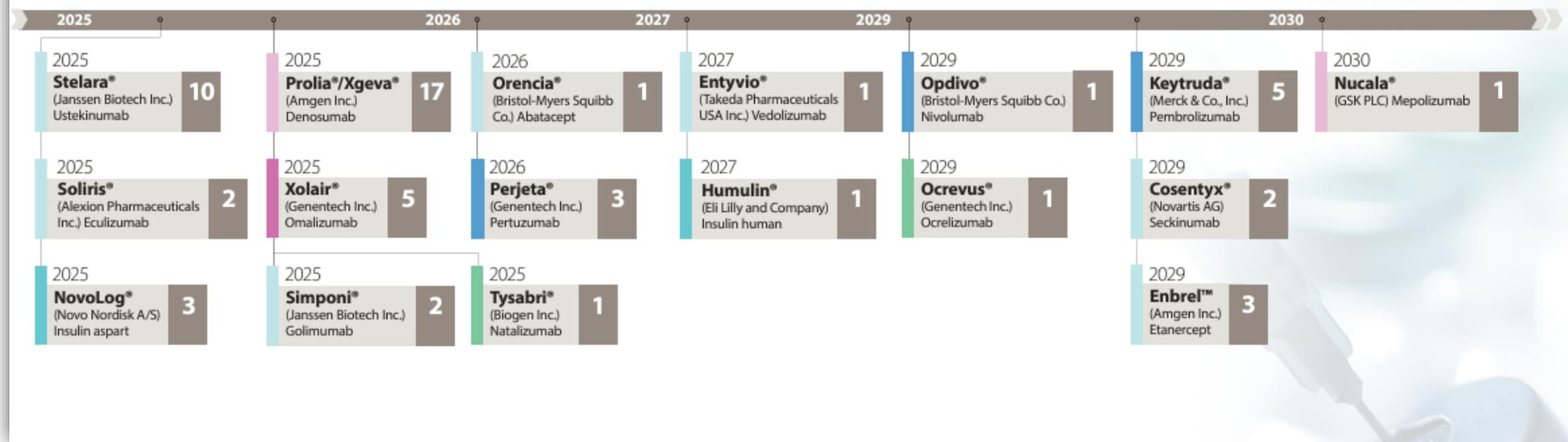
## Biosimilars timeline



Year the first anticipated biosimilar launches

**Reference biologic** (company) molecule # = Number of biosimilars either in clinical trials, pending FDA approval or FDA approved

■ Asthma   
 ■ Bone health   
 ■ Diabetes   
 ■ Immunology (i.e., RA/GI/Derm)   
 ■ Ophthalmology   
 ■ Oncology   
 ■ Supportive care   
 ■ Neurology



# Pending Legislation to Limit Patents in BPCIA Cases

## Affordable Prescriptions for Patients Act

- In a congressional spending bill that passed in the Senate, but not yet passed in the House
- Allows for the assertion of only 20 patents in litigation
- Allows exception for good cause (such as material change of reference product or patent issued late due to PTO delays)

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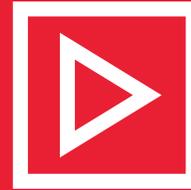
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